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Pre-clinical and clinical study on Rajarajeswaram and Madhanabiravam for anti- epileptic activity in the management of Valippu(Epilepsy)

(DISSERTATION SUBJECT)

For the partial fulfillment of the

requirement to the Degree of

DOCTOR OF MEDICINE (SIDDHA)

BRANCH II - GUNAPADAM

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BONAFIDE CERTIFICATE

Certified that I have gone through the dissertation submitted by **Dr. A.Kirubagaran,** (Reg.no:32101702) student of **final year M.D(S),** Branch-II **Department of Gunapadam**, National Institute of Siddha, Tambaram sanatorium, Chennai-47 and the dissertation work has been carried out by the individual only. This dissertation does not represent or reproduce the dissertations submitted and approved earlier.

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Date**:**

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Preclinical and clinical study on Rajarajeswaram and Madhanabiravam for anti- epileptic activity in the management of Valippu(Epilepsy)

INTRODUCTION:

Siddha system which is widely practiced in Tamilnadu,it is one of the most ancient medical system in the world. Siddhars classified diseases into 4448 types. The raw materials used for treating diseases by the Siddhars as drugs were classified into herbal, herbo-mineral, metal, inorganic,animal products and sea products. Discreption of the disease Valippu noi(Epilepsy) was taken for this research had already described by siddhars about the types ,symptoms and treatment methodology.

Epilepsy is a neurological disorder due to sudden burst of abnormal electrical discharges from the brain. Epilepsy is the second most common chronic neurological condition seen by neurologists. It has no age, racial, social, sexual or geographical boundaries.

Epilepsy affects 50 million people worldwide, and 80% of them live in the developing world. It is estimated that there are 55,00,000 persons with epilepsy in India. 3-5%of the population have a seizure sometime in their life and 0.5%-1%of the population have ‘active epilepsy’.

Epilepsy treatment responds to nearly 70% of patients, but in developing countries, three-fourths of people with epilepsy are ignorant to receive the essential treatment. In the modern medicine system anti-epileptic medicines are unaffordable, need long term medication and are having more contra-indications like sedation, mental irritation, memory loss, obesity, lethargy, poor concentration, inflammation of gums, etc. And for these above reasons, epileptic patients find it difficult to follow.

Evaluation of prevalence study indicates that more case-control studies to find out the aetiology, pharmaco-economic study to find out the affordable drug for general public and mass health education should be undertaken to dispel the social stigma and to bring about change in the attitude about the disease.

But several hundred years ago itself in the siddha system of medicine, siddhars, like Agasthiyar, found out the right diagnosis of epilepsy and proper treatment . They classified the epilepsy in to 21 types and prescribed siddha medicines for the same.

As per the literature **Agasthiyar Vaidhya Chinthamani** the symptoms of kakkai valippu are mentioned as giddiness followed by a fall with huge cry, syncope and involuntary movements of both legs and arms. As per **Sarabendrar Vadha Roga Chigichai** the symptoms are as follows "Tremors in both arms and legs followed by syncope, involuntary rotation of eye balls". According to **T.V. Saambasivam Pillai** Dictionary Kakkai Valippu is defined as "It is a disease of central nervous system characterised by uttering a strangled scream, loss of consciousness, white froths collecting on the lips and other distressing features of a dying person".In review of siddha text, Onan sudar thylam, Gandhaga sudar thylam, Jothi rishi thylam,Veepam nei and Pitchu ennai are found to be suitable medicines now prescribed by the siddha physicians for the management of epilepsy. To cite an example, in Tiruvannamalai District, in Madavalam village oil called Valippu ennai is given for the epileptic patients and this is the traditional treatment being followed for a long period of time.

For better convenience of the patient rather than oil, the scholar had prefered **Rajarajeswaram** and **Madhana biravam** tablets, and hence, chosen this subject for the dissertation work. Both the above mentioned tablets are indicated for Janni noi in Siddha vaidiya thirattu, authored Dr.K.N.Kuppusamy mudaliyar and Dr.K.S.Uhuthamarayan, published by Department of Indian medicine and Homeopathy, Govt of Tamilnadu. Seizure is one among the primary symptom of janni noi. Janni and valippu are with predominant elevation of iya kutram. These tablets contains the ingredients like minerals found in the above said of oil, and pitchi(bile) found in the oil meant for children. Hence the **Rajarajeswarm** and **Madhana biravam** were chosen as the trial drugs and these tablets have not been evaluated for anti- epileptic activity so far. Hence the study has been selected for the scientific evaluation of the trial drugs and the therapeutic efficacy in treating epilepsy.

AIM AND OBJECTIVES

AIM

To evaluate the safety and efficacy of Rajarajeswaram and Madhana biravam for anti-epileptic activity in the management of Epilepsy.

OBJECTIVES

The pre-clinical and clinical efficacy of Rajarajeswaram and Madhana biravam have been evaluated in the following aspects.

1. Review of literature.
2. Standard operative procedure
3. Bio-chemical aspect
4. Quantitative analysis and physical properties.
5. Atomic absorption spectrophotometer (AAS) for chemical characterization.
6. FTIR study.
7. SEM analysis
8. Toxicological study:

    Acute toxicity and sub-acute toxicity

9. Pharmacological study:

    Anti-epileptic activity

10. Clinical study:

    A pilot study on Rajarajeswaram and Madhana biravam.

11. Statistical analysis.

REVIEW OF LITERATURE

Ingredients of the trial drug 1: *Rajarajeswaram

The following raw drugs are the ingredients of ***Rajarajeswaram***

Rasam (Mercury)	- 35 gms.
Paal Thutham(Zinc sulphate)	- 35 gms.
Lingam(Chinnabar)	- 35 gms.
Gandagam(Sulphur)	- 35 gms.
Manosilai(Red orpiment)	- 35 gms.
Nabi(Aconitum ferox.Linn)	- 35 gms.
Vepam eerku kudineer(Azadirachta indica.A.Juss)	- 35 gms.
Pichu(Goat and he-buffalo bile)	- sufficient quantity.

Ingredients of the trial drug 2:(*Madhana biravam*)*

The following raw drugs are the ingredients of ***Madhana biravam***

Rasam (Mercury)	- 35 gms.
Gandagam(Sulphur)	- 35 gms.
Manosilai(Red orpiment)	- 35 gms.
Indhuppu(Sodium chloride impura)	- 35 gms.
Tamira parpam (Copper parpam)	- 35 gms.
Kandakathiri pazha saaru(solanum surattense Burm.f)	- 35 gms.
Pichu(Cow Bile)	- sufficient quantity.

* Siddha vaidiya thirattu, authored Dr.K.N.Kuppusamy mudaliyar and Dr.K.S.Uhuthamarayan, published by Department of Indian medicine and Homeopathy, Govt of Tamilnadu.

NAABI

English Name **:** Indian aconite

Common names **:** Indian aconite, monks hood, blue aconite

Botanical Name **:** Aconitum ferox. Linn

Family **:** Rananculaceae

Distribution : Blue aconite is found in Nepal, Kashmir, Sikkim, Bhutan at altitudes of 2000-3000 meters. It is a typical Himalayan plant and has even been observed growing at 3600 meters.

Organoleptic characters:

Taste	: Bitter
Potency	: Hot
Pirivu	: Acrid

Actions: Diaphoretic,Diuretic,Anti-periodic,Anodyne,Anti-phlogistic,Narcotic,Sedative . The root is attributed with sweat, nervine, appetite stimulatory, calming and anti-pyretic effects.

பொதுக் குணம் :

“Å¡¾Å Ä¢ Áó¾ÁÈø Á¡È¡ì ¸ÀôÀ¢½¢¸û
µÐ Ì ð¼ Ì ý Áó §¾÷ ´ Î í ¸¡ ñ - ¸¡¾Ä÷¾õ
Òò¾¢§Â¡ ¼¡ÕÂ¢Õõ â × õ Å ¨ É Ì Æ§Ä!
Íò¾¢ ¦ºö¾ ¿¡À¢Â¢ý §À÷ ¦º¡ø”.

Phyto-chemicals: Aconite root contains 0.3 to 1 percent of alkaloids like Aconitine which is crystalline, acrid and highly toxic, Benzaconine (Picraconitine) and Aconine

Uses: Internally tincture of root is used in treating fever and rheumatism. Paste of root is applied externally in case of neuralgia, rheumatism, acute gout and painful conditions.

REPORTED PHARMACOLOGICAL ACTIVITIES:

Inhibition of stimulus-triggered and spontaneous epileptiform activity **in rat hippocampal slices by the** Aconitum **alkaloid mesaconitine.**

Abstract

The aim of the present study was to investigate if the plant alkaloid, mesaconitine, which has been reported to have antinociceptive effects via stimulation of the noradrenergic system, inhibits epileptiform field potentials. The experiments were performed as extracellular recordings on rat hippocampal slices. Spontaneous epileptiform activity was elicited by perfusing a nominally Mg2+-free bathing medium with high K+ concentration (5 mM). Both stimulus-triggered and spontaneous epileptiform activity was attenuated in a concentration-dependent manner by mesaconitine (30 nM-1 microM). The inhibitory effect was rather variable in appearance when lower concentrations (30 and 100 nM) of mesaconitine were applied. Pretreatment of the slices with the alpha-adrenoceptor antagonist yohimbine (1 microM) prevented the effect of mesaconitine. It is concluded that the inhibitory action of mesaconitine at low concentration is mediated via alpha-adrenoceptors.

Bicuculline-induced epileptiform activity **in rat hippocampal slices: suppression by** Aconitum**alkaloids.**

Abstract

Alkaloids of Aconitum spec. (Ranunculaceae) are employed in traditional Chinese folk medicine as analgesics. The present study was designed in order to investigate the effects of the structurally related alkaloids aconitine, lappaconitine, and 6-benzoylheteratisine on experimentally induced epileptiform activity. Experiments were performed as extracellular recordings of stimulus evoked population spikes in rat hippocampal slices.. The present findings suggest that the structurally related Aconitum alkaloids aconitine, lappaconitine, and 6-benzoylheteratisine possess an anticonvulsive potential. The predominant effect of these alkaloids is to suppress the spread of seizure activity, and they may therefore tend to distort epileptic events. However, despite their similar structure, they exert qualitatively and quantitatively different inhibitory effects.

The effects of Aconitum **alkaloids on the central nervous system.**

Abstract

Preparations of Aconitum roots are employed in Chinese and Japanese medicine for analgesic, antirheumatic and neurological indications. The recent surge in use of phytomedicine derived from traditional Chinese medicine as well as increasing concerns about possible toxic effects of these compounds have inspired a great deal of research into the mechanisms by which certain Aconitum alkaloids may act on the central nervous system. The pharmacological effects of preparations of Aconitum roots are attributed to several diterpenoid alkaloids. The main alkaloid of these plants is aconitine, a highly toxic diterpenoid alkaloid which is known to suppress the inactivation of voltage-dependent Na+ channels by binding to neurotoxin binding site 2 of the alpha-subunit of the channel protein.

Aconitine inhibits epileptiform activity **in rat hippocampal slices.**

Abstract

The effect of aconitine, an alkaloid neurotoxin known to bind at site 2 of the sodium channel, was investigated on epileptiform activity in hippocampal slices by use of extracellular recordings in CA1 pyramidal cell layer. Epileptiform activity was induced by bicuculline, picrotoxin, penicillin, pentylenetetrazol or by omission of magnesium from the bathing medium, respectively. In every case aconitine (0.1 and 1 microM) blocked the multiple population spikes representing the epileptiform activity. The onset of inhibition was shorter by use of an increased concentration of the epileptogenic drug. Epileptiform activity evoked by pentylenetetrazol and low magnesium was first increased by aconitine followed by a rapid inhibition, while the bicuculline-, picrotoxin-, and penicillin-induced epileptiform discharges were immediately abolished

RASAM

English name : Mercury, Quick Silver

Chemical name : Hydrar gyrum

Organoleptic Characters

Taste : Six tastes – dominated by sweet

Potency : Hot and Cold

Actions : Tonic, Vitalizer, Diuretic, Silogogue, Anti inflammatory, Laxative,

Neutralizing pitha, Medicine for venereal diseases.

The Mercury is the chief of all elements. It gives good health, protects the body and cures the diseases that affect the body. Further it facilitates to attain the eight folded siddhis.

பொதுக் குணம் :

“Å¢Æ¢§¿¡ö ¸¢Ãó¾¢Ì ý Áõ ¦Áö î Ý ¨ Ä Ò ñ Ì ð
¼Æ¢¸¡Ä¢ø Å¢óÐ Å¢É¡ø « ò ¨¾ - ÅÆ¢Â¡ö
ÒÃ¢Ô Å¢¾¢ Â¡Ð ÒÃ¢Â¢§É¡ ¦Âø Ä¡õ
þÃ¢Ô Å¢¾¢ Â¡Ð Á¢ø ¨ Ä”

Proper use of Mercury as medicine cures the diseases of eyes, syphilis, eight types of ulcers (Gunmam), throbbing pain (Soolai), chronic ulcer (Perum Pun).

Beneficial properties:

- It purifies blood, it improves blood and sperms
- Kills the micro-organisms and cures the ulcers
- It cures the diseases of internal and external organs of the body
- It improves memory power, eradicates amnesia
- It strengthens the nerve plexuses
- It develops wisdom through concentration of mind
- It prevents senility and increases the life span.

Special properties:

Mercury, unlike other drugs, is useful in the treatment of diseases caused by both heat and cold.

GANDHAGAM

English name : Sulphur

Organoleptic Characters

Taste **:** Bitter and Astringent

Potency **:** Hot and Cold

Pirivu : Kaarppu (Pungent)

Actions **:** Laxative, Tonic, Antiseptic, Diaphoretic, cholagogue

Types **:** Pirappu, Vaippu, Nellikkai, Vaana

Nellikkai Gandhagam is the one which is often used in medicine preparations.

பொது குணம்:

“¦¿øÄ¢ì¸¡öì ¸ó¾¢ìÌ ¿¦ûÀ¾¢¦½ýÌð¼ Áó¾õ
Åø¨Ä ¸Å¢¨ºÌýÁ Å¡Ô¸ ñ§½¡ö - ¦À¡øÄ¡
Å¢¼ì¸Ê Åý §Á¸§¿¡ö Å¦ÚÍÃõ §À¾¢
¾¢¼ì¸¢ÃÍ ½¦¸Àõ§À¡ó §¾÷”

It is useful in the treatment of 18 types of Skin Diseases, Liver Enlargemet, Abdominal Distention, Eye Diseases, Chronic Venereal Diseases, Chronic Diarrhea, Gastric Ulcer, Poisonous Bites, Fever due to Vatham, Chronic Dysentery etc.

Special properties :

Sulphur as an internal medicine heals the diseases effectively in a way similar to that of mother’s care

LINGAM

English name : Cinnabar, Virmilion

Chemical name : Red sulphide of Mercury(Natural).

Organoleptic Characters:

Taste : Not Specific

Potency : Hot

Actions : Alterative

General properties:

“§À¾¢Í Ã ï ºó¿¢ ¦ÀÕÅ¢Ã½ ¿¦¡Ã¡ Î ¾
¸¡¾¸Ê ¸¡º ï ¸ÃôÀ¡ ý Ò ñ -§½ ¡¾
× Õ º í ¸¾Á¡ ä Ú ¸ðÊ Ôõ§À¡ í
Ì Õ Å¢Ä¢í ¸ º í ¸Áò ¨ ¾ì ¦¸¡û”

“ ¬ ¾¢ Â¢Ã¾ × Õ ì ¸¡¾Ä¡ü º¡¾¢Ä¢í ¸
§Á¡¾¢ Ä¢Ã¾ Ì ½ Óü Ú¼Ä¢ü-È¦ÐÒÃ¢
Ì ð¼í ¸¢Ãó¾¢ ¦¸¡ Î ï Ý ¨ Ä Å¡¾Ó¾ü
Ö ð¼í Ì §¿¡ö¸ ¨ Ç§Â¡ð Î õ”

It is effective in the treatment of Diarrhea, Pyrexia, Delirium, Utricaria, Diuresis, Tuberculosis, Scabies, Unkown Insect Bites, Shyphilis, Leprosy, Eczema, Skin Diseases, Throbbing Pain and Vatha Diseases.

Special properties:

It has the properties of curing the diseases caused by the earth element and cures the diseases caused by the water element.

பால் துத்தம்

English Name : zinc sulphate

வேறு பெயர்கள் : ¦Åû ¨Ç Ðò¾õ,Á¼ø Ðò¾õ, ¿¡¸×ôÒ, ¦ÅûÇ¢Â ¯ôÒ

நிறம் : ¦Å ñ ¨Á, ¿¢Ã¢ø ¸¨ÃÔõ

செய்கை : ¯¼ø ¯ÃÁ¡ì¸¢, ÐÅ÷ôÀ¢,þº¢Å¸üÈ¢, Å¡ó¾¢Ô ñ¼¡ì¸¢

பொதுகுணம் :

ÓüÈ¢Â ÌÈ¢ôÒ ñ Ó¨ÇÅ¢Ã½õ ¦ºý É¢¾¨ Éô
ÀüÈ¢¿¢ýÈ Å¡¾õ À¼÷¸ÃôÀ¡ý Íò¾ Å¢Æ¢ì
¸¡ºí¸½õ À¢øÄõ ¸ñ§½¡ö Ìó¾ò ¦¾¡¨ ÄÔõ
Å¡ºÁ¢Ì Ðò¾ò¾¡ø Å¡úòÐ.

மருத்துவ பயன்பாடுகள் :

1.Ðò¾ò¾¡ø ¯ýÁ¡ó¾õ,¸¡ì¨¸ÅÄ¢,Ý¾¸ºý É¢¿¡í Ìõ.

2.þº¢¨Å §À¡ì ÌÅ¾ü Ìõ, ¯¼Ö ì Ì Åý¨Á «Ç¢ôÀ¾ü Ìõ 65 Á¢¸¢ Å¢¾õ ¦¿ö

«øÄÐ ¦Å ñ¦½ö ¸ÄóÐ ¦¸¡Î ì¸×õ.

மனோ சிலை

English Name : Red orpiment

Arsenic disulphide is a naturally occurring form of arsenic and is found as realgar, one of the major arsenic containing mineral. Arsenic disulphide insoluble in water and so poorly absorbed. It there fore represents a much less acute toxic hazard than soluble arsenic compounds.

Synonyms: Red arsenic disulphide, Arsenic disulphide, Arsenic sulfide, Red orpiment, Ruby arsenic, Realgar.

Chemical name and formula:Arsenic disulphide(AS_2S_4)

Physical properties : Red Brown

பொது குணம் :

“ ¸¡öîºø ¿Î ì¸ø «º¸øÄ¢Ô¨ÃôÒîº¢Äó¾¢

§ÀºÚõ Á§É¡º¢¨Ä §ÀÍ “

Tradional uses :

In fever it is generally used in combination with mercury, orpiment etc . as in the following svasakuthara rasa is consisting of realgar, mercury, sulphur, aconite, borax, black pepper, ginger, and long pepper is recommended in remittent fever with cerebral complications. Dose is 4 grains in pill form.

இந்துப்பு

English Name **:Rock salt , Sodium chloride impure**

வேறு பெயர்கள் **:** ¨ ºó¾Åõ, º¢óÐ¡Ãõ, ºó¾¢Ã Û ôÒ, Á¾¢ÔôÒ, Á¾¢ì Ü÷ ¨ Á,

Á¢ó¾¡ î ¦ º¡ ø

நிறம் :§ÁüÀì ¸õ ¸À¢Ä ¿¢Èõ, ¯ðÀì ¸õ ¦Å ñ ¨ Á

செய்கை :

ÁÄ ¸¡¡¢ ¦ºö ¨ ¸

பொது குணம் :

“« ð¼ Ì ý Á Áó¾õ « º¢÷ì ¸Ã ï Ý÷ º¾À¢ò¾ó
Ð ð¼ ¨ ÅÂõ ¿¡ÊôÒ ñ §¼¡¼ í ¸û - ¦ ¸ ð¼ÁÄ ì
¸ ð Î Å¢¼ Å¢ó ¨ ¾ ¨ Âì ¸¡Á¢Â§¿¡ö Å ý ¸ÃôÀ¡ ý
Å¢ð Î Å¢¼ Å¢óÐô ¨ À Å¢û “

It is used in the treatment of 8 types of gunmam, Kaba pitham, poison intake, mutthodam, constipation, diseases of head, eye, tongue, dental roots, chin, neck and external genital organs.

USES:

1. It is used to treat many kinds of skin diseases and also to reduce pain in rheumatic ailments.

2. It is used to reduce pain, inflammation and irritation in case of insect bites. Having the right level of salt assists the body with many functions including nerve conduction.

தாமிரம்

English Name : Copper

சுவை : ¸¡÷ôÒ, ¨¸ôÒ

வீரியம் : ¦ÅôÀ Å¡¢Âõ

பிரிவு : ¸¡÷ôÒ

பொதுக் குணம் :

“¾¡õÀ¢Ãò¾¡ü §º¡¡¢ À¢ò¾õ ºó¿¢Â Ì ¨ Å ¸Àõ
Å¡õÀ¡÷ À¢Ä¢¸õ Áó¾õ, ¦Å ñ §Á¸õ, §¾õÀÆ¨ Ä
Ý¾¸§¿¡ö Ò ñ ¸¢Ãó¾¢ §¾¡¼ Í Å¡º í ¸¢ÕÁ¢
¾¡Ð¿ð¼õ ¸ ñ §¿¡ö §À¡õ º¡üÚ “

¦ºö¨¸ : þº¢Å¸üÈ¢

மருத்துவ பயன்பாடுகள் :

¾¡Á¢ÃÀüÀò¨¾¾¡Á¨Ã,« øÄ¢, ¦¸¡ðÊ þÅüÈ¢ý âîº¡Ú ²¾¡ÅÐ ´ýÈ¢ø ¾Ã¸¡ì¨¸ÅÄ¢¾Õõ.

Uses

1. Copper act as Anti-oxidant and Anti-bacterial
2. Copper is used as Immuno-modulator
3. The two radioactive isotopes of copper are used in health care.
4. Copper-64 is used to study brain function.
5. The Ebers Papyrus (c. 1500 BC) mentions the use of copper for headaches, "trembling of the limbs".
6. Copper dependent enzyme are required for normal brain development and function. deficiency can result pathological disorder accompanied by convulsive seizure or tremor in man and animal. administration of therapeutically effective amount of an organic compound of copper having anti-convulstant activity.

Copper-dependent enzymes are required for normal brain development and function.

Copper deficiency can result in pathological disorders accompanied by convulsive seizures or tremors in man and animals. The present invention is directed to a method for treating convulsions or epilepsy comprising administration of a therapeutically effective amount of an organic compound of copper having anticonvulsant activity. Those compounds include copper complexes of carboxylic acids, acylsalicylates, salicylates, amino acids, imines and known anticonvulsant and antiepileptic drugs.

Method for treating convulsions and epilepsy with organic copper compounds

Anticonvulsant Activities of Copper Complexes

The brain contains more copper than any other organ of the body except the liver. This fact suggests that copper plays a role in brain functions. With reports of seizures in animals and humans following copper-deficient diets, it was reasoned that copper has a role to play in the prevention of seizures. It was subsequently discovered that organic compounds that are not themselves anti-convulsants exhibit anticonvulsant activity when complexed with copper. Further, it was found that copper complexes of all anti-epileptic drugs are more effective and less toxic than their parent drugs. Synthesis, structural analysis and anticonvulsant activity of a ternary Cu(II) mononuclear complex containing 1,10-phenanthroline and the leading antiepileptic drug valproic acid.

Anticonvulsant properties of copper acetazolamide complexes.

Abstract

Two copper acetazolamide complexes were synthesized for evaluation as anticonvulsant agents. These complexes were found to be more effective as anticonvulsants than the acetazolamide.

பிச்சு

English Name : Bile

வேறு பெயர் : À¢òÐ

செய்கை : ÁÄÁ¢Çì¸¢

மருத்துவ பயன்கள் :

1. º ý É¢ §¿¡ö¸ Ù ì Ì ÅÆí Ìõ ¨ÀÃÅ Á¡ò¾¢¨Ã¸¨Ç «¨Ãì¸ ÀÂýÀÎ¸¢ÈÐ.
2. ¸¡ì¨¸ ÅÄ¢ì Ì À¢îº¢± ñ ¦½ö¨Â ÅÆí Ìõ Ó¨Èô ÀüÈ¢ À¡ÄÅ¡¸¼ò¾¢ø ÜÈôÀð Î ûÇÐ.

GOAT BILE

The composition of bile varies substantially with in Cholic acid – commonest acid found in bile deoxycholic acid , chenocholic acid, hyocholic acid, lithocholic acid.

Alcohols

C_{27} or c_{28} occur in the biles amphibian fish. Bile acids and alcohols normally occur in conjugated forms ,acids conjugating with the amino acids" taurine" or "glycine". Carnivore biles contain largely salts of cholic acids .

Name	Total lipids	Billirubin	Cholesterol	Fatty acid	Total bileacid
Ox	100-160	-	37	370	7200
Dog	-	92-170	80-100	1600-5000	7900-15000
Guinea pig	140	-	-	-	780
Rabbit	-	87-131	10-120	-	1100-2600
Rat	-	8-9	12.7	-	-
Pig	-	32-62	130-180	820-2000	8500-12000
Man	-	1000	630	970	5180

கண்டங்கத்திரி

English Name : Febrifuge Plant

Botanical name : Solanum surattense Burm.f

செய்கை : §¸¡¨ ÆÂ¸üÈ¢, º¢Ú¿÷ô ¦ÀÕì¸¢, «¸ð Î Å¡Â¸üÈ¢

பொதுக் குணம் :

"காசசுவாசங் கதித்தஷய மந்த மனல்
வீசு சுரஞ் சந்நி விளைதோஷ - மாசுறுங்கா
லித்தரையு ணிற்கா, ளிகாரஞ் சேர்கண்டங்
கத்தரியுண் டாமாகிற் காண் "

- அகத்தியர் குணவாகடம்

CHUKKU

Botanical name : Zingiber officinale Rosc

Family : Zingiberaceae

Parts used : Dried rhizome

Organoleptic Characters

Taste : Acrid

Potency : Hot

Pirivu : Acrid

Actions : Stimulant, Stomachic, Carminative

பொதுக் குணம் :

"Ý ¨ ÄÁó¾õ ¦¿ ï ¦ºÃ¢ôÒ §¾¡¼§ÁÔ ÀõÁÆ¨ Ä
ã Äõ þ¨ÃôÀ¢ÕÁø ã ì Ì ¿÷ - Å¡Ä¸À
§¾¡¼Á¾¢ º¡Ãó ¦¾¡¼÷Å¡¾ Ì ý Á¿÷ò
§¾¡¼õ ¬ Áõ §À¡ì Ì ï Í ì Ì"

Chemical Constituents:

Camphene, phellandrene, zingiberine, cineol, borneol, gingerol, gingerin, resin, Starch. Bisabolene, borneol, camphene, cineol, citral, citronellol, geranial, limonene,linalool, Phellandrene, zingiberene, zingiberol.

Volatile oils (bisabolene, borneol, camphene, cineol, citral, citronellol, geranial, limonene, linalool, phellandrene, zingiberene, zingiberol).

The aromatic principles are bisabolene & zingiberene, the pungent principles are gingerols & shogaols which are anti-nausea. Gingerols turn into shogaols when exposed to heat and air.

MILAGU

Botanical name	**:**	Piper nigrum.Linn
Family	**:**	Piperaceae
Parts used	**:**	Dried unripe fruit

Organoleptic Characters

Taste	:	Bitter, acrid
Potency	:	Hot
Pirivu	:	Acrid
Actions	:	Carminative, Antiperiodic, Rubefacient, Stimulant Antidote, Resolvent

பொதுக் குணம் :

“º¡¾Í Ãõ À¡ ñ Î º§Ä òÁ í ¸Ã¡ ½ Ì ý Áõ
Å¡¾õ « Õ ºÀòõ¾õ Á¡ ã Äõ-µ Ð º ý É
Â¡ºÁÀŠ Á¡Ãõ «¼Ä§Á¸õ ¸¡ºÁ ¨ Å
¿¡º í ¸È Á Ç¸ É¡ø.
§¸¡ Ï ¸ý È Àì¸ÅÄ Ì öÂ×§Ã¡ ¸õÅ¡¾
§º¡ ½ ¾ í ¸ Ø ò¾ü Ì û §¾¡ ý Ú§¿¡ö-¸¡ ½ Ã Â
¸¡Ð§¿¡ö Á¡¾÷ Ì ý Á í ¸¡Á¡ ¨ Ä Áó¾¦ Á ý È÷
²Ð§¿¡ö ¸¡Â Õ ì¸ ø ® í Ì.”

மிளகின் பெருமை:

"¾¢Â¡¸¢ ¦Â í Ì õ ¾¢Ã¢ÔÁ ¨ ¾ Â¡Å òÐ
§Á¡Â¡Á ¦ÄôÀÊÔ Ó ñ ¼¡ì ¸¡ü-À¡Â¡Ð
§À¡ó¾¢Á¢÷Å¡ ¾í ¸¢Ãó¾¢ Ò ñ ½¦Õõ Á ñ ½ Å÷ì Ì õ
¸¡ó¾¢¦ÁöÅ¡ ¾îºÖô ¨ Àì ¸¡ö."

- தேரன் வெண்பா

Á¢Ç Ì, ÅÇ¢, ¾¢, ¸Àì ÌüÈ í ¸û « ¨ É ò ¨ ¾Ôõ ¿¦ì Ì õ. « ý È¢Ôõ ¾¢Á¢÷Å¡¾õ, ¸Æ¨ Ä, ÅÇ¢, ºÇ¢ ¬ ¸¢ÂÅü ¨ È « ¸üÚõ.

Phytochemicals: Piperine, piperidine.

The principle ingredients of Piper nigrum are dimeric amide alkaloids with cyclohexene ring, nigramides, dimeric amide alkaloids with cyclobutane ring, nigramides P-S.

Uses:

It is useful in treating cold, cough, fever, gastric ulcer, haemorrhoids, vatha diseases, etc. It is an effective antidote.

Chemical Constituents:

Chavicine, piperine, piperidine, essential oil, safrol, tannic acid, piperamide, pyrrolidine, piperolein – b, balsamic volatile oil.

THIPPILI

Botanical name	:	Piper longum Linn
Family	:	Piperaceae
Parts used	:	Dried unripe fruit
Organoleptic Characters		
Taste	:	Acrid
Potency	:	Hot
Pirivu	:	Sweet
Actions	:	Stimulant and Carminative

பொதுக் குணம் :

“ ¬ º É §¿¡ö ¦¾¡ ñ ¨¼ §¿¡ö ¬ ÅÃ½ À¢ò¾Ó¾ø
¿¡º¢Å¢Æ¢ ¸¡¾¢¨ Å§¿¡ö ¿¡ðÒØ§¿¡ö - Å¦º¢ Î Å¢
Â í ¸Ä¡ ï º É ï º¢¨ ¾Ôõ « õÀ¡ö « Æ¢Å¢óÐõ
¦À¡ í ¸Ä¡ ï º ¿ í ¨ ¸Â÷§¸¡ð §À¡ø”

Chemical Constituents:

Resin, Volatile Oil, Starch, Fatty Oil, Piperine. The fruits contain 1% volatile oil, resin, a waxy alkaloid, a terpenoid substance and alkaloids piperine and piperlongumine

VEMBU

English Name **:** Neem

Botanical Name **:** Azhadirachta indica.A.Juss.

Family **:** Meliaceae

Parts used **:** Leaf, unripe fruit, ripe fruit, seed

Organoleptic characters:

Taste : Bitter

Potency : Hot

Pirivu : Acrid

Phytochemicals **:**Margosine

Activities **:**timulant, Anthelmintic, Discutient, Antiseptic, Insecticide

பொதுக் குணம் :

“Å¡¾õ§À¡õ À¢ò¾Á¢Ì õ Á¡È¡ì¸¢ÃÓ¾¦Â¡ Î
§Á¡Ð¸Ãô À¡ý º¢Ãí Ì Óý É¢º¢×õ -´Ð¼Ä¢ý
¿¡ôÀ Ï ÚÍÃÓ ¿¡ Î º ý É¢Ôó¦¾¡¨ ÄÔõ
§Åôà¦¿ö ¦Âý ¦È¡Õì¸¡ø Å¢û Ù”.

அகத்தியர் குணவாகடம்

Effects of piperine on convulsions and on brain serotonin and catecholamine levels in E1 mice.

Convulsions of E1 mice were completely suppressed by 60 mg/kg of piperine injected intraperitoneally. The ED50 was 21.1 mg/kg. The brain 5-HT, dopamine and norepinephrine levels were estimated 1 hour after the intraperitoneal injection of piperine. The 5-HT level was significantly higher in the cerebral cortex of piperine treated mice than in control mice. This increase may be related directly to the mechanism of inhibition of convulsions by piperine. On the other hand, lower levels of 5-HT were observed in the hippocampus, midbrain and cerebellum. The dopamine level in the piperine treated mice was markedly higher only in the hypothalamus, while the norepinephrine levels were lower in every part of the brain.

A review of pharmacology and clinical use of piperine and its derivatives

Piperine and its derivatives are effective anticonvulsant drugs that antagonize convulsions induced by physical and chemical methods. Their major anticonvulsant activity as shown in animal tests lies in modification of the maximal electroshock seizure pattern. They also have sedative-hypnotic, tranquilizing, and muscle-relaxing actions and can intensify the depressive action of other depressants, when used in combination. Antiepilepsirine, one of the derivatives of piperine, is used as an antiepileptic drug in treating different types of epilepsy. It has been proved effective and is being widely used in China. The anticonvulsant action of 7446, 7448, and 7903 is more potent than that of antiepilepsirine. The chemical structure of piperine and its derivatives is different from that of prototype antiepileptic drugs, and, therefore, these may become a new group of antiepileptic drugs.

Anticonvulsant activity of piperine on seizures induced by excitatory amino acid receptor agonists.

In traditional Chinese medicine, a mixture of radish and pepper is used to treat epilepsy. The presumptive effectiveness of this prescription might be due to the anticonvulsant actions of the principal component of pepper, the alkaloid piperine (CAS 94-62-2). The effects of piperine on convulsions induced in mice by agonists at different excitatory amino acid receptor subtypes were studied. Piperine was shown to significantly block convulsions induced by intracerebroventricular injection of threshold doses of kainate, but to have no or only slight effects on convulsions induced by L-glutamate, N-methyl-D-aspartate or guanidinosuccinate. Piperine suspensions, injected intraperitoneally, 1 h before injection of the threshold intracerebroventricular dose of kainate for the induction of clonic convulsions (1 nmol), blocked these convulsions with an ED50 (and 95% confidence interval) of 46 (25-86) mg/kg. Although piperine did block convulsions, induced by kainate, the compound does not appear to act as a kainate receptor antagonist. Whole-cell currents induced by the application of kainate to spinal cord cells in primary dissociated cultures were not affected by co- application of piperine.

Diet

The ketogenic diet, which includes high amounts of fat and very low amounts of carbohydrates, is an age-old treatment for epilepsy that has been revived in recent years. The diet effectively reduces seizures for some people, especially children, but it is difficult to maintain.

Researchers are trying to learn exactly how the ketogenic diet prevents seizures. They hope to find ways to chemically mimic its seizure-blocking effects without the dietary restrictions.

Several studies have suggested that substances called beta-hydroxybutyrate (BHB) and acetoacetate, which increase in people who follow the ketogenic diet, play a role in blocking seizures.

Other researchers used a chemical called 2-deoxy-D-glucose (2DG) to block carbohydrate breakdown in a rat model of epilepsy. This chemical reduced the expression of genes involved in epilepsy and reduced the number and severity of seizures in the rats. If this substance works in people, it might be the basis for a new class of antiepileptic drugs.

Studies are examining which types of seizures and epilepsy syndromes respond best to the ketogenic diet. Studies have shown particularly good results with infantile spasms, pyruvate dehydrogenase deficiency, and glucose transporter protein deficiency. The diet is also useful for some people with other forms of epilepsy.

Several clinical studies are now testing whether the high-protein Atkins diet and other diets that are less extreme than the ketogenic diet may help to reduce seizures.

வலி நோய்

வேறு பெயர்கள் :

þØôÒ, þº× §¿¡ö

இயல்பு :

þó§¿¡ö «È× Ì ýÈò ¾ý ¿¨Ä Á¡ÚÀð Îò ¾ý ¨ÉÂÈÂ¡Á§Ä ¨¸Ôí ¸¡Öõ ÅÄòÐ þØò¾ø, Å¡Âø Ñ¨Ã ¾ûÇø, Å¡ö §¸¡½ì ¦¸¡û Ù¾ø ,¸ñÀ¡÷¨Å ´ÕÒÈÁ¡¸ þØòÐì ¦¸¡ûÇø ±ýÛõ þÂøÒ¨¼Â¾¡õ.

நோய் தோன்றும் வழி :

þó§¿¡Â¡ÉÐ §Á¸§¿¡öì Ìò ¦¾¡¼÷À¡¸ ÅÕõ ±É×õ, ¯¼ø ¿¨ÄÔõ ÁÉ ¿¨ÄÔõ ¦¸Î¾Ä¡Öõ ÅÕõ ±É×õ, «¨Å ³Âò¨¾ Á¢Ì¾ôÀÎòÐõ ¯½Å¡¾¸Ç¡Öõ ¦Àñ½¢î¨ºÂø Á¢Ì¾Ôõ ®ÎÀ¼ø, ¦ÀÕõ «È¢»÷¸¨Çô ÀÆò¾Ä¡¸Â¿¼ò¨¾¸Ç¡Öõ ¯ñ¼¡Ì¦ÁÉì ÜÈÔûÇ¡÷¸û.

நோய் எண் :

´Õ º¡Ã¡÷ þ¾¨É ³Å¨¸ ÅÄ¢ ±É×õ, Áü¦È¡Õ º¡Ã¡÷ þ¾¨É þÕÀò¦¾¡Õ Å¨¸Â¡¸×õ À¢¡òÐûÇ¡÷¸û.

(1) ஐவகை வலி நோய்களாவன:

1.ÓôÀ¢½¢ÅÄ¢ (ÌÁÃ¸ ñ¼ý)

2.Ì¾¢¨Ã ÅÄ¢ («ÁÃ¸ ñ¼ý)

3.ÌÃí Ì ÅÄ¢ (À¢ÃÁ¸ ñ¼ý)

4.¸¡ì¨¸ ÅÄ¢

5.ÓÂø ÅÄ¢ (ÓÂÄ¸ý) ±ýÀ¨ÅÂ¡õ.

(2) þÕÀò¦¾¡Õ Å¨¸ ÅÄ¢ §¿¡ö¸Ç¡ÅÉ :

1. «ÁÃ¸ ñ¼ý ÅÄ¢

2. Ì ÁÃ¸ ñ¼ý ÅÄ¢

3. À¢ÃÁ¸ ñ¼ý ÅÄ¢

4. ¸¡ì ¨ ¸ ÅÄ¢

5. ÓÂø ÅÄ¢

6. ¾¢Á÷ ÅÄ¢

7. §¸¡Û ÅÄ¢

8. º ñ ¼¡Ç ÅÄ¢

9. ÁÃ½ ÅÄ¢

10. Á§É¡ ÅÄ¢

11. ¿ ï Í ÅÄ¢

12. Ó ì Ì üÈ ÅÄ¢

13. ³Â ÅÄ¢

14. Å¢ø ÅÄ¢ (¾Û÷ ÅÄ¢)

15. ÍÃ ÅÄ¢

16. Å¢ì¸ø ÅÄ¢

17. ¾¨Ä ÅÄ¢

18. §¸¡¨Æ ÅÄ¢

19. µÎ ÅÄ¢

20. Á¡÷Ò ÅÄ¢

21. ¾ÁÃ¸ ÅÄ¢ ±ýÀ¨Å¸Ç¡õ.

காக்கை வலி

1. º¡üÈ¢§É¡õ ¸ ñ ¸ ¨ ÇÔ ÁÄÃô À¡÷ì Ì õ
º¡ í ¸Á¡ö ÁÄºÄÓ ï ºÕ ¸¢ Å¢Øõ
Á¡üÈ¢§É¡ ï º¢§Ä ð Î Áò¾¢ø À¢Èó¾ §Ã¡ ¸õ
ÁÂì ¸Ó¼ý ¸¡ø ¨ ¸ ¸û Ó ¨ ÈòÐì ¦ ¸¡û Ù õ
Ü üÚÅÉ¡ó ¦¾¡ ñ ¨¼¾É¢ø §¸¡ ¨Æ §º÷óÐ
Ì È¢ôÀ¡É ¿¡×ÄÃø Ì Ç¡¢ô §À Í õ
¸¡üÈ¢É¢Ö õ §Å¸Á¾¡ö ´ ðÊì ¦ ¸¡øÖõ
¸¡Ä É¡í ¸¡ì ¨ ¸ÅÄ¢ ¾ý ¨ Á Â¡§Á

2. «È¢Ô í ¸¡ì ¨ ¸ ÅÄ¢¾¡ Û õ
« ÄÕõ ¸ ñ Ï õ §Áø §¿¡ì ¸¢
À¢¡Ô ÁÄÓ ï ºÄ¿¦Õõ
¦ÀÕ ¸¢ì ¸¡üÚ ¨¼Ô Á¼ì ¸¡Áø
¦ ºÈ¢Ôó ¦¾¡ ñ ¨¼ ¿¡× Ä÷óÐ
º¢§Ä òÁõ Á¢ ï º¢ì ºÇ¢§Å÷ ¨ Å
Ì È¢Â¡õ Å¡¾ À¢ò¾ ¨ ÁÂ í
¦ ¸¡ ñ ¼ º ý É¢ Â¢Ð¾¡§É

±ýÈ¾¡ø, þó§¿¡Â¢ø « Ä ñ Î « Ä ñ Î ÀÂôÀ Î ¾ø, ¸ ñ ¸û §Áø§¿¡ì ¸¢ ÁÄÃ ÁÄÃ Å¢Æ¢ò¾ø, ¦¾¡ ¨¼Â¡ É Ð Á¼ì ¸ ÓÊÂ¡Áø Å¢¨ È òÐì ¦ ¸¡ûÇø, ¦¾¡ ñ ¨¼Ôõ ¿¡× õ ¯ Ä÷¾ø, ³ Âô ¦ÀÕì ¸¢É¡ø ¦¾¡ ñ ¨¼Â¢ø §¸¡ ¨Æ ¸ðÊì ¦ ¸¡ ñ Î « ¾ ¨ É ì ¸ì Ì ¾ø, º¢Ú¿¦Õõ ÁÄÓõ « ¾¢¸Á¡ ¸ô §À¡¾ø, Å¢Â÷ ¨ Å Ô ñ ¼¡¾ø Ó¾Ä¢Â Ì È¢ Ì ½ í ¸ ¨ Çô ¦ÀÚõ. þó§¿¡ö ³ Âì Ì üÈò¾¡ø À¢È ì Ì ¦ÁÉ¢Ûõ º ý É¢À¡¾ì Ì È¢ Ì ½ í ¸ ¨ Ç ¯ ñ ¼¡ì Ì õ. §¿¡ö ÅÕõ§À¡Ð Ó¸ò ¨ ¾ì ¸¦ú§¿¡ì ¸¢ ¨ Åò Ðô À Î ôÀÃ¡õ.

வலி நோயின் பொதுக் குறிகுணங்கள் :

ÅÄ¢ §¿¡ö ¦ÀÕõÀ¡ý ¨ÁÔõ º¢Ú ÅÂ¾ø ÅÕÅ¾¡Ìõ. ¿Î ÅÂÐ Å¨Ãì Ìõ º¢ÄÕì Ì ¿¢ÊôÀÐ ñ Î. ¿¡üÀÐ ÅÂÐ Å¨Ãì Ìõ ¿¢¨ÄôÀÐÓ ñ Î. ¨¸ì ÌÆó¨¾¸Ù ì Ì ÅÕõ ÅÄ¢ Àý É¢Ã ñ Î «øÄÐ À¾¨ÉóÐ ÅÂÐ Å¨ÃÂ¢Öõ Å¢ð Î Å¢ð Î ÅÕÅÐÓ ñ Î.

º¢ÄÕì Ìô §Àº¢ì ¦¸¡ ñÊÕì Ìõ§À¡§¾¡ ²§¾Ûõ §Å¨Ä ¦ºöÐ ¦¸¡ ñÊÕì Ìõ§À¡§¾¡ ¾Ë¦ÃÉ ÅÄ¢§¿¡ö ÅÕÅÐ ñ Î. º¢ÄÕì Ì ÅÄ¢ ÅÕÅ¾ü Ì Óý§À ÅÄ¢ ÅÃô§À¡¸¢ýÈÐ ±ý Ûõ ¯½÷îº¢¨Â ¯ ñ¼¡ì¸¢, Á¢Ìó¾ º¢Éõ, ÁÂì¸õ, ÁÉî§º¡÷×, §º¡õÀø, Á¢Ìó¾ Àº¢, ¦ÅÕ ñ¼ À¡÷¨Å ¬¸¢Â ÌÈ¢Ì ½ í¸¨Çì ¸¡ðÊ þØôÒ ¦¾¡¼Õõ.

«ýÈ¢Ôõ «Êì¸Ê ÐõÓ¾ø, ¦¸¡ð¼¡Å¢ Å¢¼ø, ¯¼Ä¢ý º¨¾ ÐÊò¾ø, ÁÂì¸õ, ¯½÷îº¢ÂüÚì ¸¢¼ò¾ø, º¢Ú¿¡÷ ¸Æ¢Â¡¾¢Õò¾ø, Å¡Â¢ø Ñ¨Ã¾ûÇÄ¡¸¢Â ÌÈ¢Ì ½ í¸¨ÇÔõ ¦ÀÚõ. º¢Ä ¿¡Æ¢¨¸ ¦ºýÈÀ¢ý ¦¾Ç¢óÐ ±Øó¾¢ÕôÀ÷. º¢Ä ºÁÂõ þùÅÄ¢Â¡ÉÐ ±Ç¢¾ø Å¢ðÎ Å¢ÊÛõ ´Õ ¿¡¨ÇìÌô ÀýÓ¨È ÅÕÅÐ ñ Î «øÄÐ ¿¡û ¸½ì¸¢ýÈ¢ ¿¢¨Éò¾ §À¡¦¾øÄ¡õ ÅÄ¢ ÅÕÅÐ ñ Î. ´Õ ¿¡¨ÇìÌô ÀýÓ¨È «Îò¾ÎòÐ ÅÄ¢ ÅóÐ ¦¸¡ ñÊÕôÀ¢ý §¿¡ö ÓüÚõ ¦¾Ç¢óÐ ¿¢¨É× ¯ ñ¼¡Å¾üÌî ºüÚ ¾¡Á¾Á¡Ìõ.

ÁüÚõ º¢Ä þØôÒ¸Ç¢ø ¨¸ ¸¡ø¸Ç¢ý Å¢Ãø¸û ¦¸¡ÚìÌ ÅÄ¢ §À¡ø Á¼í¸¢ò ÐÊôÒ ñ¼¡Ìõ. ¾¨ÄÔí¸ñ Ïõ ´Õ ÒÈò§¾ þØìÌõ. «È¢× Ì¨ÈóÐ ÁÂì¸Ó ñ¼¡Ìõ. ¨¸Ôí¸¡Öõ Á¼ì¸ ÓÊÂ¡Áø Å¢¨ÈòÐ ¯¾Úõ. ¸ñ Å¢Æ¢òÐì ¦¸¡ ñ§¼Â¢Õì¸î ¦ºöÔõ. ¯½÷îº¢¨Âì ¦¸Îò Ð, ¯¼¨Äô À¢ý Ûõ Óý Ûõ Å¨ÇòÐ þØòÐì Üì ÌÃÄ¢Îõ. Å¡ö §¸¡½Ä¡Ìõ. Àü¸Êì Ìõ. ¿¡¨Åì ¸ÊòÐì ¦¸¡ûÙõ, ãîÍò ¾¢½Úõ, ¦¾¡ ñ¨¼ ¸ðÎõ, ¯¼ø ¸ÚòÐô§À¡õ. Å¡Â¢ø Ñ¨ÃÔõ ÌÕ¾¢Ôõ ¸ÄóÐ ¦ÅÇ¢Â¡Ìõ. ãì¸Ä¢ÕóÐõ ÌÕ¾¢ ¸º¢ÅÐÓ ñ Î. þùÅ¡Ú ¦¸¡Î¨Á¸û ÀÄ ¦ºöÐ, º¢Ä ¿¡Æ¢¨¸ì Ì û ÅÄ¢ Ì¨ÈóÐ ¦¸¡ ñ§¼ ÅóÐ, À¢È Ì ¯½÷îº¢ ¦ÀüÚ ±Øó¾¢Õì¸î ¦ºöÔõ. ÅÄ¢ Å¢ðÎ ±Øó¾ §À¡¾¢Öõ ¾¡í¸ ÓÊÂ¡¾ ¾¨Ä ÅÄ¢Ôõ §º¡÷×õ Ð¡ì¸Óõ ±Øõ.

ºt Ä÷ Å Ä t Å ó¾ § À ¡ Ð Ó ¸ ò ¨ ¾ ì ¸ t ú Ò È Á ¡ ¸ , ¾ ¨ Ã § Á Ä ¡ ¸ t Ö õ , À Î ì ¨ ¸ § Á Ä ¡ ¸ t Ö õ ¨ Å ò Ð ì ¦ ¸ ¡ û Å ÷ . þ ¨ ¾ ì ¸ ¡ ì ¨ ¸ Å Ä t ¦ Â É ì Ü Ú Å ÷ . þ ù Å Ä t þ Ã Å t ø Ð ¡ í Ì õ § À ¡ Ð Å ¡ t ý ºt Ä § Å ¨ Ç Á Ã ½ ò ¨ ¾ Ô õ ¯ ñ ¼ ¡ ì Ì õ ± ý À ÷ .

Á ü Ú õ ºt Ä Õ ì Ì þ ù Å Ä t Â t ø ºt Ú ¿ ¦ ÷ ¾ ý ¨ É Â È t Â ¡ Á § Ä þ Æ t Å Ð Ó ñ Î . Å Ä t ì ¦ ¸ ¡ Î ¨ Á Â ¡ ø ºt Ä º Á Â õ ¯ ¼ õ À t ø « Ê À ð Î Å ¦ í Ì ¾ ø , ¸ ¡ Â Ó ñ ¼ ¡ ¾ ø , ± Ö õ Ò ¸ û Ó È ¦ ¾ ø , ¯ ¼ ø Ó Ø ¨ Á Ô õ § ¿ ¡ ¾ ø , Ì Õ ¾ t Å ¡ ó ¾ t Â ¡ ¾ ø Ó ¾ Ä t Â Ì È t Ì ½ í ¸ ¨ Ç Ô õ Å t ¨ Ç Å t ì ¸ ì Ü Î õ . § ¿ ¡ Â t ý ¦ ¸ ¡ Î ¨ Á ì § ¸ ü À þ ó § ¿ ¡ Ô ¼ ý À ì ¸ Å ¡ ¾ Ó õ (À ¡ ¡ t º Å ¡ Ô , À ì ¸ Å ¡ Ô) ¦ ¾ ¡ ¼ Õ Å Ð ñ Î .

Ì Æ ó ¨ ¾ ¸ Ù ì Ì Å Õ õ § ¿ ¡ Â t ø , § ¿ ¡ ö Å Õ Å ¾ ü Ì Ó ý § À Í Ã í ¸ ¡ ö ó Ð Å t Ã ø ¸ û Ð Ê ô À Ð õ , ¨ ¸ ¸ ¡ ø ¸ Ç t ý º ¨ ¾ ¸ û Ð Ê ô À Ð Á ¡ ¸ Â t Õ ó Ð « ô À ¡ ø Ì Æ ó ¨ ¾ ¾ ¡ í ¸ Ó Ê Â ¡ ¾ þ Ø ô ¨ À Å Õ Å t ì Ì õ . ¦ À Õ õ À ¡ Ö õ Ì Æ ó ¨ ¾ ¸ Ç t ø Á Ä î º t ì ¸ Ö ¼ ý º ¦ ¾ Ó ñ ¼ ¡ ö î Í Ã õ ¬ Ã õ À t ì Ì õ Ó ý É ¾ ¡ ¸ § Å ¦ À ¡ t Â Å ÷ ¸ Ù ì Ì Í Ã õ Å Õ Ó ý Ì Ç t Õ õ ¿ Î ì ¸ Ö Ó ñ ¼ ¡ Å Ð § À ¡ Ä , Ì Æ ó ¨ ¾ ¸ Ç t ø § Á ü Ü È t Â þ º t × ± ý Û õ þ Ø ô Ò ¯ ñ ¼ ¡ Ì ¦ Á ý À ¨ ¾ ¿ t ¨ É × À Î ò ¾ t ì ¦ ¸ ¡ û Ç × õ . Í Ã õ « ¾ t ¸ ô À Î õ § À ¡ Ð þ º t × õ « Ê ì ¸ Ê ¯ ñ ¼ ¡ ¸ t º ý É t ¨ Â Ô õ À t È ô À t ì ¸ ì Ü Î õ . þ ù Å t º t × Ì Æ ó ¨ ¾ ¸ Ç t ø ´ Õ ¿ ¡ ¨ Ç ì Ì ô À Ä Ó ¨ È ¸ û Å Õ Å Ð ñ Î . Å Ä t Å Õ õ § À ¡ ¦ ¾ ø Ä ¡ õ ¸ ñ ¸ û § Á ø § ¿ ¡ ì ¸ t þ Ø ò Ð ì ¦ ¸ ¡ û Ù õ . Å ¡ ö § ¸ ¡ ½ t ´ Õ Ò È Á ¡ ¸ Å Ä t ò Ð ì ¦ ¸ ¡ û Ù õ . ¾ ¨ Ä ´ Õ À ì ¸ Á ¡ ¸ ò ¾ t Õ õ À t Â t Õ ò ¾ ø , ¿ ¡ × õ ´ Õ Ò È Á ¡ ¸ þ Ø ò Ð ì ¦ ¸ ¡ û Ç ø ± ý Û õ Ì È t Ì ½ í ¸ ¨ Ç Ô õ ¸ ¡ ð Î õ . Ì Æ ó ¨ ¾ ¸ Ù ì Ì ñ ¼ ¡ Ì õ Å Ä t § ¿ ¡ Ô ¼ ý º t Ä º Á Â õ “ À ì ¸ Å ¡ ¾ Ó õ ” À t È ô À Ð ñ Î . º t Ä Ì Æ ó ¨ ¾ ¸ Ç t ø ¸ ñ À ¡ ÷ ¨ Å Ì ¨ È Å Ð õ , ¸ ñ ¦ º ¾ ÷ Å Ð õ (« ¾ ¡ Å Ð ´ Ç t Á Ø í Ì ¾ ø ² ü À Î õ) ¯ ñ Î .

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MODERN ASPECT

EPILEPSY

Definition :

A seizure is any clinical event caused by an abnormal electrical discharge in the brain, epilepsy is the tendency to have recurrent seizure. Epilepsy should be regarded as a symptom of brain disease rather than a disease itself. A single seizure is not epilepsy but an indication for investigation , and medication should generally be withheld until recurrent seizures occur.

WHO Defines Epilepsy as “a disorder of the brain characterized by an endurg predisposition to generate Epileptic seizures, and by the neurological, cognitive, psychological and social consequences of this condition”. A Transient occurrence of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

- Epilepsy is common in children with IQ less than 50.
- Many of the inherited,idiopathic epilepsies – due to mutations affecting ion channel functions.
- Whereas mutations observed in symptomatic epilepsies – neuronal homeogenesis or CNS

  development.

- 1 in 200 of general population have epilepsy.
- The brain is built up of many billions of nerve cells, *the neurons.*

  The function of the neurons is to send out electrical impulses which pass from neuron to neuron with the help of chemical "*messengers*", the neurotransmitters.

- When the electrical impulse reaches the end of a neuron, a chemical substance is released which sets off a reaction in the "*receiver area*", a so-called synapsis in the next nerve cell. This enables the electrical impulse to travel on through this cell to the next

In this way electrical impulses are transmitted along the innumerable neuron chains which are found in the brain

CAUSES OF EPILEPSY

Neonates (< 1 month)

- Perinatal hypoxia and ischemia
- Intracranial hemorrhage and trauma
- Acute CNS infection
- Metabolic disturbances (hypoglycemia,hypokalemia,hypomagnesemia,pyrodoxin deficiency)

Infants and children (>1 month and <12 years)

- Febrile seizures
- Genetic disorders(metabolic,degenarative,

  primary epilepsy syndromes)
- Developmental disorders, trauma.
- Idiopathic

Adolescents (12-18 years)

- Illicit drug use
- Trauma
- Genetic disorders

- Brain tumor
- Infections
- Idiopathic

Young adults (18-35 years)

- Trauma
- Alcohol withdrawal
- Illicit drug use
- Idiopathi
- Brain tumour

Older adults (>35 years)

- Cerebro vascular diseases
- Brain tumor
- Alcohol withdrawal
- Metabolic disorders (uremia, hepatic failure, electrolyte abnormalities, hypoglycemia)
  Alzheimer's disease

CLASSIFICATION OF EPILEPSY

INTERNATIONAL CLASSIFICATION OF EPILEPTIC SEIZURES:

I. Partial seizures

A. Simple partial seizures

I**. With motor signs**

(a). Focal motor without march

(b). Focal motor with march (Jacksonian)

(c). Versive

(d). Postural

(e). Phonatory

II. **With somato sensory or special-sensory symptoms**

(a.) Somato sensory

(b) Visual

(c) Auditory

(d) Olfactory

(e) Gustatory

(f) Vertiginous

III**. With autonomic symptoms or signs**

IV. **With psychic symptoms**

Dysphasia

Cognitive

Affective

Illusions

B. Complex partial seizures

1. Simple partial seizures at onset, followed by impairment of consciousness

2. With simple partial features

3. With automatisms

C. WITH IMPAIRMENT OF CONSCIOUSNESS AT ONSET

(a) With impairment of consciousness only

(b) With automatisms

C. PARTIAL SEIZURES EVOLVING TO SECONDARILY GENERALIZED SEIZURES

1. Simple partial seizures evolving to generalized seizures

2. Complex partial seizures evolving to generalized seizures

3. Simple partial seizures evolving to complex partial seizures evolving to generalized

seizures

II. Generalized seizures

A. Absence seizures

1. Typical absence seizures

(a) Impairment of consciousness only

(b) With mild clonic components

(c) With atonic components

(d) With tonic components

(e) With automatisms

(f) With autonomic components

2. Atypical absence seizures

B. Myoclonic seizures

C. Clonic seizures

D. Tonic seizures

E. Tonic-clonic seizures

F. Atonic seizures

PARTIAL EPILEPSY

- Partial seizures or focal seizures are due to a small epileptic focus in the brain.
- They are of 2 types:

1.Simple partial – Seizure start as a focal discharge and remains focal throughout (without altered consciousness)

2.Complex partial – seizures start as a focal discharge (altered consciousness)

SIMPLE PARTIAL SEIZURES

- Have motor,sensory,autonomic or psychic manifestations.
- Simple partial motor seizures – discharging epileptic focus in the opposite frontal lobe (motor cortex).

Jacksonian epilepsy – clonic contractions start in fingers of one hand, one side of the face or the foot and slowly spread to the other muscles on the same side of the body

COMPLEX PARTIAL SEIZURES

- In this seizures consciousness is lost or impaired.
- They are frequently due to epileptic discharges in the temporal or frontal lobes.
- This forms the single most common type of seizures in adults.
- Temporal lobe origin – auditory or visual hallucination, sometimes olfactory or gustatory hallucinations may be present.

GENERALIZED SEIZURES

- **TONIC CLONIC SEIZURE:**

  Also called as grand mal epilepsy.

4 Stages of Grandmal Epilepsy

1.prodromal phase

2.Tonic phase

3.clonic phase

4.postictal phase

PRODROMAL PHASE:

Starts several hours before fits.

It consists of subjective phenomenon like depressed or apathetic mood, irritability, vague abdominal cramps which is easily recognized by the patients.

Sometimes the patient gets the attack without any forewarning.

TONIC PHASE:(10-30 seconds)

It consists of rolling up of the eyes associated with stiffening of the limbs Clenching of the jaws

Often resulting in injury to the tongue.

Epileptic cry – since entire musculature goes in to spasm forcing air through the closed vocal cord

CLONIC PHASE: (1-2 minutes)

It is characterized by alternate flexion-extension movements of all the four limbs convulsions).

Strenuous breathing, sweating

Frothing of the mouth and excessive salivation.

Urine and feces may be voided.

Followed by comatose state(5 minutes)

POST ICTAL STATE:

In this state the patient does not remember anything that had happened.

Pupils begin to react and the patient then resumes speech, but still remains confused.

Patient starts sleeping for several hours, often wakes up with severe headache and at times vomiting

ABSENCE SEIZURES

- Known as petit mal seizures
- Seen mostly in children
- It is distinguished by brevity and absence of motor phenomenon.

- Vacant stare – child abruptly stops all ongoing motor activity and speech. External stimuli fail to evoke any response from the patient.(2-10seconds).

ATONIC SEIZURES

- Less common generalized seizures characterized by sudden loss of postural tone and consciousness without any other motor phenomena.

This has to be distinguished from cataplexy

PATHO PHYSIOLOGY

- Pathology consists of:

1.Cell death

2.Axonal sprouting

3.Reorganisation of neural networks

4.Alteration in the release of neuro transmitters.

EPILEPSY IN CEREBRAL HEMORRHAGE OR STROKE

- CAUSE:

Hemorrhage and stroke in brain - cause destruction of brain tissue - formation of scars -irritate the surrounding nerve tissue.

- FREQUENCY:

Starts late in life.

10-15% persons with cerebral hemorrhage and stroke later develops epilepsy.

- SEIZURE TYPE:

Simple partial and secondary generalized type are common.

EPILEPSY AND HEAD TRAUMA

- CAUSE:

During trauma - brain may lack oxygen due to pinching of blood vessels - seriously irritate the nerve cells - epilepsy.

- FREQUENCY:

  10-15% of persons with head trauma

  Risk depends on age and force of blow.

- SEIZURE TYPE:

  Temporal lobe-complex partial seizure

  Few cases-status epilepticus.

EPILEPSY AND BRAIN TUMOR

- CAUSE:

  Triggered by irritation from a tumor

- FREQUENCY:

  Beginning late in life-suspicion of tumor.

  Begins after age of 25.

- SEIZURE TYPE:

  Simple partial seizure-more common.

  Complex partial seizure.

EPILEPSY AND INFLAMMATION OF THE BRAIN

- CAUSE:

  Infections-acute phase

  Bacterial meningitis-encephalitis-brain abscess. Healed brain TB often causes epilepsy due to built up of tumor like tissue which later calcifies.

  Parasites can cause fluid filled cysts in brain (cysticercosis)-exert pressure on surrounding brain tissues.

- FREQUENCY:

  4% - Bacterial meningitis

  Depends on age – Viral meningitis

- SEIZURE TYPE:

  Simple partial seizures.

  Generalized convulsions.

EPILEPSY AND MENTAL RETARDATION

- CAUSE:

  Congenital brain damage

  Hereditary brain disease

  Metabolic abnormalities

  Chromosome fault

- FREQUENCY:

  20-30% of all mentally retarded people suffer by epilepsy.

EPILEPSY AND MULTIPLE SCLEROSIS

- CAUSE:

  Might be caused by viral infection which could have occurred many years before.

- FREQUENCY:

  5 – 10 %

- SEIZURE TYPE:

  Partial seizures.

EPILEPSY AND ALCOHOL

- CAUSE:

  "Kindling"- Give a person alcohol then stop – he develops withdrawal symptoms – Give them alcohol again – Repeat it many times – their seizure threshold gradually decrease – so they starts developing seizure even without alcohol withdrawal.

- SEIZURE TYPE:

  Abstinense convulsions.

DIAGNOSIS

1.EEG

2.MRI Scan

3.PET Scan (Positron Emission Tomography)

4.SPECT (Single Photon Emission Tomography)

5.Neuro Imaging- provides views of brain areas involved in seizure activity.

6.Electrolyte disturbances.

EPILEPSY AND GABA

- Seizure occur when the message delivering system becomes unbalanced.
- GABA-neurotransmitter trigers signals.
- When there is not enough GABA,a person has seizure because the receiving neurons is flooded with signals.

EPILEPSY AND SERUM PROLACTIN

- " Serum prolactin level increases 10-20 minutes after suspected event, it should considered a useful adjunct to differentiate general tonic clonic seizure or complex partial seizure from psychogenic seizure among adult and older children."

- American academy of neurology.

WBC COUNT IN EPILEPSY

- Peripheral White Blood cell Count increases after generalized seizure and is probably transient in nature.

- pub med

SEIZURES WHICH ARE NOT EPILEPSY

1.Single seizures (stress convulsions)

2.Low blood sugar

3.Fainting.

4.Heart disease

4.Reduced blood supply to brain.

5.Migraine

6.Kinking of blood vessels

7.Narcolepsy

8.Abstinence seizures.

PROGNOSIS

- Over 60% of patients attain remission,which is defined as freedom from seizures for 2-5 years after stopping their anti epileptic treatment.
- 30%- self limiting or remit after short course of treatment.
- 30%- easily controlled with drugs
- 20%- chronic epilepsy which responds partially to drugs…

MANAGEMENT OF EPILEPSY

- PRIMARY MEASURES:

1.Treatment of acute convulsions.

2.Prophylactic management

- SECONDARY MEASURES:

1.Removal of precipitating factors.

2.Anti epileptic medications.

3.Social rehabilitations.

FIRST AID FOR AN EPILEPSY PATIENT

- The patient is put on soft bed to avoid injuries.
- Tight clothing is loosened and the airway is protected.
- Foreign bodies in the mouth should be removed and a suitable mouth gag is applied in the position of molar teeth.
- The patient should be kept with head low, to avoid aspiration.

MATERIALS AND METHODS

Trial drug 1:(Rajarajeswaram)

Collection of raw drugs:

The raw drugs(Rasam, Thutham,Lingam,Gandagam,Manosilai and Nabi) were brought from the raw drug market and pichu(goat and he-buffalo)Collected from slaughter house. All above drugs were identified and authenticated by Head of the Gunapadam Department, National Institute of Siddha, chennai-47.

1. METHOD OF PURIFICATION AND PREPARTION

Rajarajeswaram :(Internal)

Ingredients:

Rasam	-105 Gms
Thutham	-105 Gms
Lingam	-105 Gms
Gandagam	-105 Gms
Manosilai	- 105 Gms
Nabi	-105 Gms
Vepam eerku kudineer	- 850Ml
Pichu(goat and he-buffalo)	- 260 Ml

Purification process:

Rasam(Mercury):

Rasam -105 gms,Brick powder-require quantity , turmeric powder-require quantity kuppaimeni juice-3.9 litre.Mercury is triturated with brick powder and turmeric powder for one hour respectively and washed with water. Then the mercury was boiled with the juice of kuppaimeni until it was detoxified.

Paal thutham(Zinc sulphate)

The paal thutham was placed in cow's urine and heated. It was then washed with water and dried in sunshade to get purified.

Lingam(Red sulphide of mercury);

Lime juice, cows milk and the kuppaimeni juice are mixed in equal proportion and allowed to fuse lingam so as to get it in a consolidated potency state.

Gandagam(Sulphur)

The kalkam of maruthani was mixed in cows curd and placed in a mud pot the mouth of the pot was covered with a cloth. Sulphur was placed over this cloth. The pot was covered with another pot and buried in the ground. The outer pot was subjected to puda with five dung cake. The sulphur which melted and settled down is collected. This procedure was reprated for seven times.

Manosilai(Red orpiment)

Manosilai was is triturated withginger juice for 3 hours. It was then dried to get purified form.

Naabi(Aconitum ferox);

The Naabi was placed in cow's urine and put in sun light for seven days. It was then washed with water and dried to get purified.

Preparation of the medicine:

The equal amount of purified Rasam, purified Paal thutham, purified Lingam, purified Gandagam, and purified Manosilai were grounded by stone motor and pestle into fine powder and put together ,then grounded by stone motor and pestle until well mixed and then added vepam eerku kudineer mixed it and grinded and make villai and dry it. After drying then put in to mud agal and covered with mud agal then covered the edges by seelaiman. Then heated by 50 dried dungcake. After cool it mix with purified Nabi and pichu(goat and he-buffalo) and grinded two days each. Then make a kuligai the size of kundri((100-110mg).

LABELLING:

Name of the preparation	: **Rajarajeswaram**
Quantity of the drug	: 205gram
Colour	: Black
Date of manufacture	: 24.06.2012
Dose	: 100-110mg
Adjuvant/ vehicle	: Thirikadugu kudineer
Indication	: Valippu
Date of expiry	: 23.06.2013

STANDARD OPERATING PROCEDURE

Trial drug 2:(Madhana biravam)

Collection of raw drugs:

The raw drugs(Rasam,Gandagam,copper,Manosilai and Indhuppu) were brought from the raw drug market and pichu(cow bile)Collected from slaughter house. All above drugs were identified and authenticated by Head of the Gunapadam Department, National Institute of Siddha, chennai-47

METHOD OF PURIFICATION AND PREPARTION

Madhana biravam:(Internal)

Ingredients:

Rasam	-105 Gms
Gandagam	-105Gms
Manosilai	- 105 Gms
Induppu	- 105 gms
Tamira parpam	-105 Gms
Siru vazhuthunai juice	- 600 Ml
Pichu(cow)	- 260Ml

Purification process:

Rasam(Mercury):

Rasam -105 gms,Brick powder-require quantity , turmeric powder-require quantity kuppaimeni juice-3.9 litre. Mercury was triturated with brick powder and turmeric powder for one hour respectively and washed with water. Then the mercury was boiled with the juice of kuppaimeni until it was detoxified

Gandagam (Sulphur)

The kalkam of maruthani was mixed in cows curd and placed in a mud pot. The mouth of the pot was covered with a cloth. Sulphur was placed over this cloth. The pot was covered with another pot and buried in the ground. The outer pot was subjected to puda with five dung cake. The sulphur which melts and settles down was collected. This procedure was repeated for seven times.

Manosilai(Red orpiment)

Manosilai was triturated with ginger juice for 3 hours. It was then dried to get purified form.

Indhuppu (Rock salt);

The Rock salt was kept soaked in vinegar (old rice fomented water) for three days and isolated to get purified and detoxified form.

Thamira Parpam (Yakoopu Vaithya chindamani 700) :

Raw copper plate was made in to a thin blade by heating and beating then dipping in the juice of Nochi leaves(Vitex negundo) previously mixed with camphor. The process was repeated with pirandai (Cissus quadrangular) juice and butter milk. Purified Ganthagam (purified sulphur) weighing one-fourth by weight of copper blade mixed added and ground vigorously in kalvam then vallarai (Centella asiatica) juice was added and ground continuously. Then the semisolid dough like material was made in to villai. After the drying of villais, they were placed in mud pot and then sealed with mud cloth and fired in a pudam with 500 cowdung cakes. Then the villais were ground in kalvam. Fine ash coloured powder without shining was attained. This was stored in a glass container for usage.

Preparation of the medicine:

The equal amount of purified Rasam, purified Gandagam, purified Manosilai, purified Indhuppu, and tamira parpam were grounded by stone motor and pestle into fine powder and put together ,then grounded by stone motor and pestle until well mixed and then added siru vazhuthunai juice mix it and grinded and make villai and dry it. After drying then put in to mud agal and cover with mud agal then cover the edges by seelaiman. Then heated by 100 dried dungcake. After cool it mix with pichu(cow) and grinded. Then make a kuligai in the size of jute seed

Labelling:

Name of the preparation	: **Madhana Biravam**
Quantity of the drug	: 220 grams
Colour	: Pale brown
Dose	: 50-55 mg
Adjuvant/ vehicle	: Thirikadugu kudineer
Indication	: Valippu
Date of manufacture	: 16.06.2012
Date of expiry	: 15.06.2013

EVALUATION OF TABLETS

The formulated tablets were evaluated for the following physicochemical characteristics

General appearance

The formulated tablets were assessed for its general appearance and observations were made for shape, color, texture and odor.

Uniformity of weight

20 tablets were selected and were weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for tablets and none by more than double that percentage.

Disintegration Time*

Results:

S.NO	Name of the tablets	Colour	Uniformity of weight	Disintegration Time
1	Rajarajeswaram	Black	110 mg	No disintegrate
2	Madhana biravam	Pale brown	55 mg	7 minutes 10 sec

***sargam laboratory pvt ltd, Guindy,Chennai.

CHEMICAL ANALYSIS

Preparation of extract:

5 gram of Rajarajeswaram and Madhana biravam tablets are weighed separately and placed in separate 250 ml clean beakers and added with 50 ml of distilled water. Then they are boiled well for about 10 minutes seperately. Then they are is cooled and filtered in a 100 ml volumetric flasks and made up to 100 ml with distilled water respectively.

S. no	Experiment	Observation	Inference	*Rajarajeswaram*	*Madhana Biravam*
1.	Test for Sulphate a.2 ml of the above prepared extract is taken in a test tube and 2 ml of 4 % ammonium oxalate solution is added	Cloudy appearance/ white precipitate is obtained	Presence of sulphate	Present	Present
	b.2 ml of sodium carbonate extract is added with 2 ml of dilute hydrochloric acid until the effervescence ceases off. Then 2 ml of Barium Chloride solution is added	A white precipitate insoluble in concentrated Hydrochloric acid is obtained	Presence of sulphate is confirmed	Present	Present
.	Test for chloride 2 ml of Sodium Carbonate extract is added with diluted Nitric acid until the effervescence ceases. Then 2 ml of silver nitrate solution is added.	Cloudy white precipitate completely soluble in excess of Ammonium hydroxide solution is obtained	Presence of chloride is confirmed	Present	Present
.	Test for Phosphate 2 ml of the extract is treated with 2 ml of Ammonium molyhdate solution and 2 ml of concentrated Nitric acid	Presence of yellow precipitate / cloudy appearance with yellow color is obtained	Presence of Phosphate	Absent	Absent

.	Test for Carbonate 2 ml of the extract is treated with 2 ml of Magnesium Sulphate solution	Cloudy appearance / white precipitate is obtained	Presence of Carbonate is confirmed	Absent	Present
.	Test for Sulphide 1 gram of the substance is treated with 2 ml of concentrated Hydrochloric acid	Colourless, rotten egg smelling gas turning lead acetate paper black on warming evolves	Presence of Sulphide is confirmed	Present	Absent
.	Test for Nitrate 1 gram of the substance is heated with copper turnings and concentrated sulphuric acid and viewed the test tube vertically down	Copious evolution of reddish brown gas	Presence of Nitrate	Absent	Absent
.	Test for Flouride and Oxalate a.2 ml of the extract is added with 2 ml of dilute acetic acid and 2 ml of Calcium Chloride solution and heated	Cloudy appearance / white precipitate is obtained	Presence of Flouride and Oxalate	Present	Present
.	8.Test for Nitrite 3 drops of the extract is placed on a filter paper, on that 2 drops of dilute acetic acid and 2 drops of dilute Benzidine solution is placed.	No characteristic changes	Absence of Nitrite	Absent	Absent
9	Test for Borate 2 pinches of the substance is made in to paste by using sulphuric acid and added 95 % and introduced in to blue flame	Green tinged flame is seen	Presence of Borate is confirmed	Absent	Absent

S.no	Experiment	Observation	Inference	*Rajarajeswaram*	*Madhana Biravam*
1.	Test for Lead 2 ml of the extract is added with 2 ml of potassium iodide solution	Yellow precipitate soluble in hot water and reappearing as golden yellow spangles on cooling is obtained	Presence of lead is confirmed	Absent	Absent
2.	Test for Copper a.one pinch of the substance is made in to paste with concentrated hydrochloric acid in watch glass and introduced in to the non luminous part of the flame	Bluish green colored flame is obtained	Presence of Copper	Absent	Present
	b.2 ml of the extract is added with excess of Ammonia solution	Bluish precipitate or deep blue colored solution is obtained	Presence of Copper is confirmed	Absent	Present
3.	Test for Aluminium To 2 ml of the extract Sodium Hydroxide solution is added in drops to excess	White precipitate soluble in excess of Sodium Hydroxide is obtained	Presence of Aluminium is confirmed	Absent	Absent
4.	Test for Iron a.To 2 ml of the extract 2 ml of Ammonium Thio cyanate solution is added	Blood red color is obtained	Presence of Ferric Iron is confirmed	Absent	Absent
	b.To 2 ml of the extract 2 ml of Ammonium Thiocyanate solution and 2 ml of concentrated Nitric acid is added	Blood red color is obtained	Presence of Ferrous iron is confirmed	Absent	Absent
5.	Test for Zinc To 2 ml of the extract Sodium hydroxide solution is added in drops to excess and dilute ammonium chloride is added.	White precipitate soluble in excess of Sodium Hydroxide is obtained	Presence of Zinc is confirmed	Present	Absent

6.	Test for Calcium 2 ml of the extract is added with 2 ml of 4 % ammonium oxalate solution	Cloudy appearance / white precipitate is obtained	Presence of Calcium is confirmed	Present	Present
7.	Test for Magnesium To 2 ml of the extract Sodium Hydroxide solution is added in drops to excess	White precipitate insoluble in excess of Sodium Hydroxide solution is obtained	Presence of Magnesium is confirmed	Present	Absent
8.	Test for Ammonium To 2 ml of the extract few ml of Nessler's reagent and excess of Sodium Hydroxide solution are added	Reddish brown precipitate is obtained	Presence of Ammonium is confirmed	Absent	Absent
9.	Test for Pottasium A pinch of the substance is treated with w 2 ml of Sodium Nitrate solution and then treated with 2 ml of Cobalt Nitrite in 30 % glacial acetic acid	Yellowish precipitate is obtained	Presence of Potassium is confirmed	Absent	Absent
10.	Test for Sodium 2 pinches of the substance is made in to paste by using Hydrochloric acid and introduced in to blue flame	Yellow flame is seen	Presence of Sodium is confirmed	Present	Absent
11.	Test for Mercury 2 ml of the extract is treated with 2 ml of Sodium Hydroxide solution	Yellow precipitate is obtained	Presence of Mercury is confirmed	Present	Present
12.	Test for Arsenic 2 ml of the extract is treated with 2 ml of Silver Nitrate Solution	Yellow precipitate / Brownish red precipitate is obtained	Presence of Arsenic is confirmed	Present	Present

s.no	Experiment	Observation	Inference	*Rajarajeswaram*	*Madhana Biravam*
1.	Test for Starch 2 ml of the extract is treated with weak Iodine solution			Absent	Absent
2.	Test for Reducing sugar 5 ml of Benedict's qualitative solution is taken in a test tube and allowed to boil for 2 minutes and 8 – 10 drops of the extract is added and again it is boiled for 2 minutes. The color changes are noted	Change in color light green / dark green / brick red is obtained	Presence of reducing sugar	Present	Absent
3.	Test for Alkaloids a. 2 ml of the extract is treated with 2 ml of potassium iodide solution	Red color develops	Presence of Alkaloids	Present	Absent
	b.2 ml of the extract is treated with 2 ml of picric acid	Yellow color develops	Presence of Alkaloids	Present	Absent
	c.2 ml of the extract is treated with 2 ml of Phosphotungstic acid	White precipitate develops	Presence of Alkaloids	Present	Absent
4.	Test for Tannic Acid 2 ml of the extract is treated with 2 ml of Ferric Chloride solution	Black precipitate is obtained	Presence of Tannic acid	Absent	Absent
5.	Test for Unsaturated Compound: 2 ml of extract treated with 2 ml of dilute Potassium permanganate solution is added.	Potassium permanganate is not decolorized.	Absence of Unsaturated Compound	Present	Absent
6.	Test for Albumin 2 ml of the extract is added with 2 ml of Esboch's reagent	Yellow color precipitate is obtained	Presence of Albumin	Absent	Absent

PHYSICO-CHEMICAL ANALYSIS

The sample of ***Rajarajeswara kuligai and Madhana biravam*** was analyzed as per the standard guidelines.

Physico-chemical parameters

The procedures recommended in WHO guidelines (Anonymous, 1998) were followed to determine loss on drying at 105°C, total ash, acid-insoluble ash and solubility in alcohol and water

Loss on Drying of the sample at 105^0C

About 4 g of the plant powder was accurately weighed in a tarred 100 ml beaker. It was heated in a hot air oven at 105°C for 5 hours. The beaker was cooled in a esiccator and weighed. The procedure was repeated to get constant weight. The percentage of loss in weight of the sample was calculated.

Calculation

$$\text{Percentage of loss on drying at } 105\ ^0\text{C} = - \frac{\text{Loss in weight of the sample}}{\text{Weight of the sample taken}} \times 100$$

Total ash content

About 4 g of the plant powder was accurately weighed in a previously ignited and tarred silica dish. The sample was ignited in a muffle furnace at 600°C to convert completely into ash. The dish was cooled in a desiccator and weighed. The procedure was repeated to get constant weight. The percentage of total ash was calculated.

Calculation

$$\text{Percentage of total ash} = \frac{\text{Weight of the ash}}{\text{Weight of the sample taken}} \times 100$$

Acid insoluble ash

To the dish containing total ash, 15 ml of 1: 5 hydrochloric acid was added thrice and gently heated for 5 minutes and filtered through Whatman No: 41 filter paper. The filter paper along with the insoluble matter was transferred to silica dish and ignited in a muffle furnace at 600°C to get constant weight. The dish was cooled in desiccator and weighed. The percentage of acid insoluble ash was calculated.

Calculation

$$\text{Percentage of acid-insoluble ash} = \frac{\text{Weight of the acid insoluble residue}}{\text{Weight of the sample taken}} \times 100$$

Water soluble extractive

About 4 g of the plant powder was accurately weighed in glass stoppered 250 ml flask. 100 ml of distilled water was added and shaken occasionally for 6 hours and then allowed to stand for 18 hours. The solution was filtered using Whatman No:1 filter paper. 25 ml of the filtrate was pipetted out into a preweighed 100 ml beaker. The filtrate was evaporated on a water bath and the beaker was dried in a hot air oven at 105°C for 6 hours. It was cooled in a desiccator and weighed. The percentage of the water soluble extractive was calculated.

Calculation

$$\text{Percentage of water soluble extractive} = \frac{\text{Weight of the extract}}{\text{Weight of the sample taken}} \times \frac{100}{25} \times 100$$

Alcohol soluble Extractive

About 4 g of the plant powder was accurately weighed in glass stoppered 250 ml flask. 100 ml of distilled alcohol (95%) was added and shaken occasionally for 6 hours and then allowed to stand for 18 hours. The solution was filtered using Whatman No: 1 filter paper. 25 ml of the filtrate was pipetted out into a preweighed 100 ml beaker. The filtrate was evaporated on a water bath and the beaker was dried in a hot air oven at 105°C for 6 hours. It was cooled in a desiccator and weighed. The percentage of the water soluble extractive was calculated.

Calculation

$$\text{Percentage of alchohol soluble extractive} = \frac{\text{Weight of the extract}}{\text{Weight of the sample taken}} \times \frac{100}{25} \times 100$$

Estimation of the heavy metals.

The procedures recommended for analysis of Heavy Metals like Lead, Cadmium, Mercury and Arsenic in WHO, 1998 and AOAC, 2005.

Instrument & Operating parameter

Thermo Fisher M Series, 650902 V1.27 model atomic absorption spectrometer (AAS) was used in the analysis. The operating parameters for:

Instrument details:

Thermo Fisher M Series, 650902 V1.27 model **A**tomic Absorption Spectrometer (AAS) was used for the analysis. The operating parameters:

Lead and Cadmium:

Instrument technique	: Flame technique
Wavelength (Lead)	: 217 nm
Wavelength (Cadmium)	: 228.8 nm
Slit width	: 0. 5 mm
Lamp current (Pb)	: 4.0 mA
Lamp current (Cd)	: 3.0 mA
Carrier gas and flow rate	: Air and Acetylene, 1.1 L/min
Flow rate	: 2 ml/min

Mercury:

Instrument technique	: Cold vapour technique
Wavelength	: 253.7 nm
Slit width	: 0. 5 mm
Lamp current	: 3.0 mA,
Carrier gas and flow rate	: Argon, 1.1 L/min
Flow rate	: 5ml/min

Arsenic:

Instrument technique	:	Flame vapour technique
Wavelength	:	193.7 nm
Slit width	:	0. 5 mm
Lamp current	:	6.0 mA,
Carrier gas and flow rate	:	Acetylene, Argon, 1.1 L/min
Flow rate	:	5ml/min

The Hallow cathode lamp for Pb, Cd, Hg and As analysis were used as light source to provide specific wavelength for the elements to be determined.

Preparation of sample solutions

Cadmium and Lead

Take 5 g of the sample in a pre-weighed silica dish. Add 5 ml of digestion mixture (Nitric acid: Perchloric acid 2 : l) and heat slowly to 100°C and maintain at this temperature for 3 hours. Raise the temperature very slowly to 240°C avoiding losses due to possible violent reactions especially in the temperature range of 160°C to 200°C an maintain at this temperature till it becomes dry (approximately 4 hours). Dissolve the remaining inorganic residue in 20 ml nitric acid make it up to 100 in a volumetric flask with distilled water.

Mercury

Weigh 5 gms of the sample into a digestion flask. Add 25 ml of 9M sulphuric acid, 20ml of 7M Nitric acid, 1 ml 2% Sodium Molybdate solution and 5-6 boiling chips.Connect the condenser and apply gentle heat for 1 hour. Allow it cool. Add 20 mlNitric acid-Perchloric acid (1:1) through the condenser. Boil until white fumes appear in the flask. Cool and add cautiously 10 ml of water through the condenser. Again boil the solution for l0 minutes. Cool and wash the condenser with three 15 ml portions of water, cool the solution to room temperature. Transfer the digest to 100 ml volumetric flask and make up to the mark with deionised water.

Arsenic

Take 5 g of the sample in kjeldal flask and add 10 ml of de-ionized water. 25 ml of concentrated Nitric acid and 20 ml of Concentrated Sulphuric acid. Heat cautiously so that no excessive foaming takes place. Gradually add concentrated Nitric acid drop by drop until all the organic matter is destroyed. If darkening of the solution is observed, add some more Concentrated Nitric acid with continuous heating until a clear solution is obtained. Cool and add 30 ml of de-ionised water and 10 ml of Ammonium oxalate (25 g/l) solution. Heat again until copious white fume is evolved. Cool and make up to 100 ml in a volumetric flask with de-ionized water.

Analysis of Aflatoxins

The procedures recommended for analysis of Aflatoxins B_1, B_2, G_1 and G_2 as per Official Analytical Methods of the American Spice Trade Association (ASTA), 1997.

Instrument details:

Thermo Fisher High Performance Liquid Chromatography (HPLC) was used in the Aflatoxins analysis. The operating parameters:

Column **:** Ultra C18, 250 X 4.6 mm, 5 µm particles

Mobile Phase **:** Water: Acetonitrile: Methanol (65: 22.5: 22.5)

Flow rate **:** 1 mL/min.

Temperature **:** 35º C

Detector **:** Fluorescence detector at 360 nm

Injection **:** 20 µl (Aflatoxins mixture and Sample)

RESULTS AND DISCUSSION

Evaluation of tablets

The formulated tablets ***Rajarajeswara kuligai and Madhana biravam*** were evaluated for the physicochemical characteristics.

Uniformity of weight

Uniformity of weight of ***Rajarajeswara kuligai*** was observed as 110mg and ***Madhana biravam*** was observed as 55mg

1. Physico-chemical values

S. No.	Parameter	RajaRajeswaram	*Madhana biravam*
1.	Loss on drying at 105^{o}C	6.37 %	4.19 %
2.	**Ash values**		
	a. Total Ash	58.62 %	87.93 %
	b. Acid Insoluble Ash	3.78 %	15.34 %
3.	**Extract Values**		
	a. Alcohol	5.16 %	8.70 %
	b. Water	26.32 %	49.45 %

2. Analysis of Heavy Metals

S. No.	Name of the Element	RajaRajeswaram	*Madhana biravam*	Permissible Limit
1	Lead	0.1635 ppm	0.1977 ppm	10 ppm (WHO)
2	Cadmium	Not Detected	Not Detected	0.3 ppm (WHO)
3	Mercury	0.8024 ppm	0.7137 ppm	1 ppm (API, 2008)
4	Arsenic	0.1732 ppm	0.1836 ppm	3 ppm (API, 2008)

3. Analysis of Aflatoxins

S. No.	Aflatoxins	RajaRajeswaram	*Madhana biravam*
1	B_1	Not detected	Not detected
2	B_2	Not detected	Not detected
3	G_1	Not detected	Not detected
4	G_2	Not detected	Not detected

4.Analysis of Microbial Load

The procedures recommended for analysis of Microbial Load as per WHO, 1998.

S. No.	Parameters	RajaRajeswaram	*Madhana biravam*	Permissible Limit for Internal use
1	Total Bacterial Count (TBC)	$\leq$ 10 CFU/g	$\leq$ 10 CFU/g	10^5 CFU/g
2	Total Fungal Count (TFC)	$\leq$ 10 CFU/g	$\leq$ 10 CFU/g	10^3 CFU/g
3	Enterobacteriaceae	Absent	Absent	10^3 CFU/g
4	*Escherichia coli*	Absent	Absent	10 CFU/g
5	Salmonella Spp	Absent	Absent	Absent
6	*Staphylococcus aureus*	Absent	Absent	Absent

FTIR STUDY

In order to prepare a **KBr pellet**, follow the procedure given below:

Sample/KBr ratio

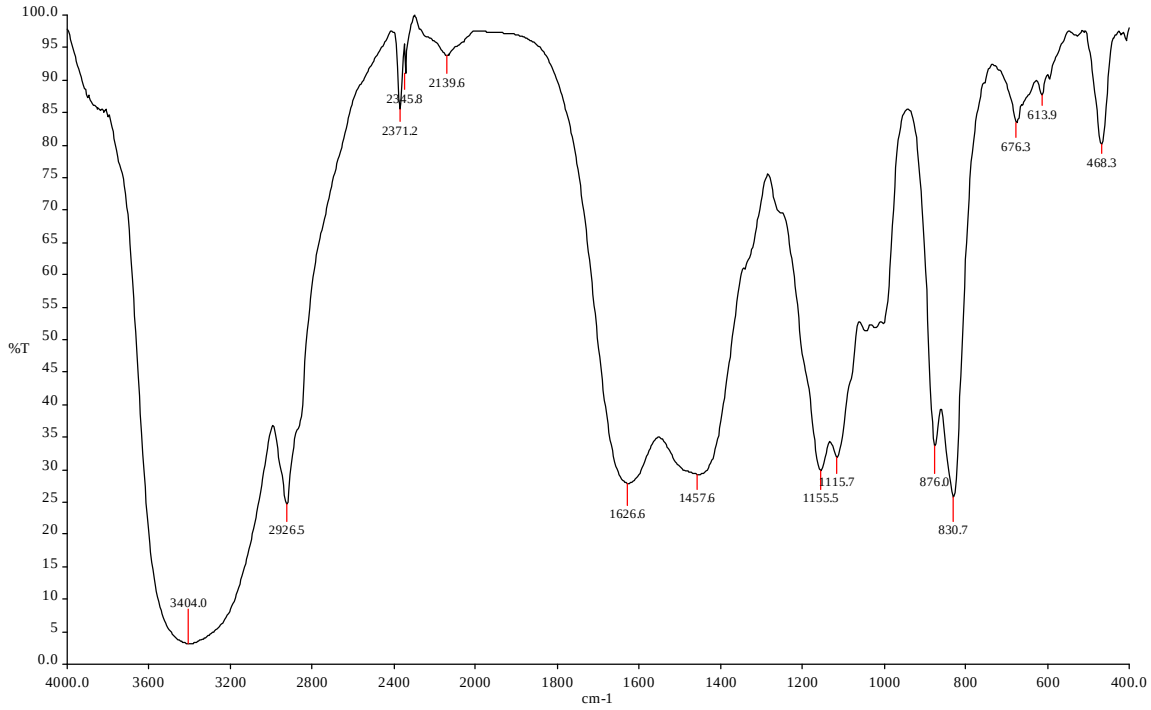
The concentration of the sample in KBr should be in the range of 0.2% to 1%. The pellet is much thicker than a liquid film, hence a lower concentration in the sample is required (Beer's Law). Too high a concentration usually causes difficulties obtaining clear pellets. The IR beam is absorbed completely, or scattered from the sample which results in very noisy spectra.

Sample preparation

Although a homogeneous mixture will give the best results, excessive grinding of the potassium bromide is not required. The finely powdered potassium bromide will absorb more humidity (it is hygroscopic) from the air and therefore lead to an increased background in certain ranges. Make sure to work fast. Transfer some KBr out of the oven (ATTENTION: the oven is at 100 ^{o}C - you can easily burn yourself!) into a mortar. Add about 1 to 2 % of your sample, mix and grind to a fine powder. For very hard samples, add the sample first, grind, add KBr and then grind again.The sample must be very finely ground as in the Nujol mulling technique to reduce scattering losses and absorption band distortions.

Take two stainless steel disks out of the desiccator. Place a piece of the precut cardboard (in the tin can next to the oven) on top of one disk and fill the cutout hole with the finely ground mixture. Put the second stainless steel disk on top and transfer the sandwich onto the pistil in the hydraulic press. With a pumping movement, move the hydraulic pump handle downward. The pistil will start to move upward until it reaches the top of the pump chamber. Then, move the pump handle upwards and pump until the pressure reaches 20,000 prf. Leave for a few seconds and with the small lever on the left side, release the pressure (hold until the sample and pistil are all the way down). Remove the disks and pull apart. Remove the film, which should be homogenous and transparent in appearance. Insert into the IR sample holder and attach with scotch tape. Run the spectrum.

After use, the mortar and pistil should be cleaned with acetone and double distilled water, and be put back on top of the oven for drying.



Rajarajeswarm pk

REF 4000 97.9 2000 97.5 600

3404.0 3.1 2926.5 24.6 2371.2 85.6 2345.8 91.0 2139.6 93.8

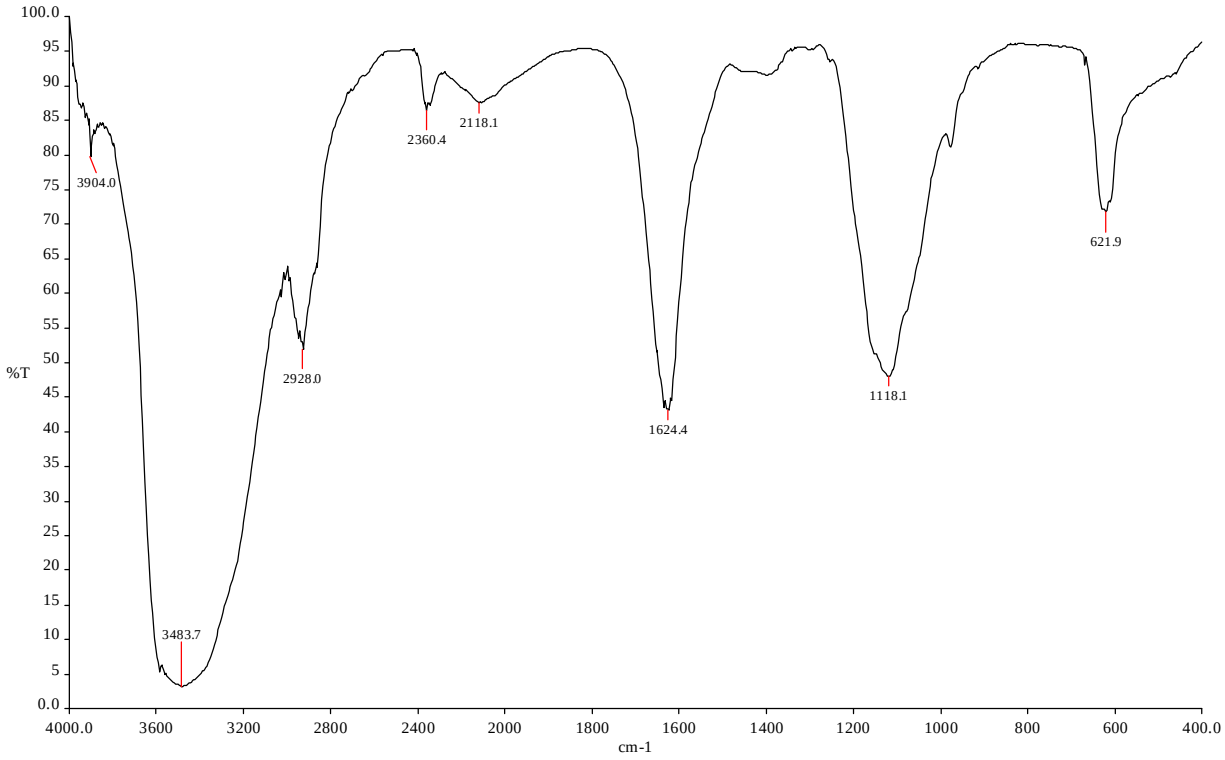
1626.6 27.8 1457.6 29.2 1155.5 29.8 1115.7 31.7 876.0 33.5

830.7 25.7 676.3 83.4 613.9 87.6 468.3 80.1

END 14 PEAK(S) FOUND

IR Spectra – Interpretation:

The IR spectrum showed the presence of hydroxyl group (3404 cm^{-1}), ester carbonyl (2926.5 cm^{-1}), trisubstituted double bond (1626.6 and 830.7 cm^{-1}), aromatic function (1457.6 cm^{-1}) and C-O stretching (1155.5 cm^{-1}).



Madhana biravam.pk

REF 4000 100.0 2000 90.1 600

3904.0 79.8 3483.7 3.1 2928.0 51.9 2360.4 86.3 2118.1 87.4

1624.4 43.1 1118.1 48.0 621.9 71.7

END 8 PEAK(S) FOUND

IR Spectra – Interpretation:

The IR spectrum showed the presence of hydroxyl group (3483.7 cm^{-1}), ester carbonyl (2928 cm^{-1}), trisubstituted double bond (1624.4 cm^{-1}) and C-O stretching (1118.1 cm^{-1}).

SOPHISTICATED ANALYTICAL INSTRUMENT FACILITY

ANNA UNIVERSITY,CHENNAI

SEM-METHODOLOGY

An SEM is essentially a high magnification microscope, which uses a focussed scanned electron beam to produce images of the sample, both top-down and, with the necessary sample preparation, cross-sections. The primary electron beam interacts with the sample in a number of key ways:-

- Primary electrons generate low energy secondary electrons, which tend to emphasize the topographic nature of the specimen.
- Primary electrons can be backscattered which produces images with a high degree of atomic number (Z) contrast.
- Ionized atoms can relax by electron shell-to-shell transitions, which lead to either X-ray emission or Auger electron ejection. The X-rays emitted are characteristic of the elements in the top few μm of the sample.

SAMPLE PREPARATION:

Sample preparation can be minimal or elaborate for SEM analysis, depending on the nature of the samples and the data required. Minimal preparation includes acquisition of a sample that will fit into the SEM chamber and some accommodation to prevent charge build-up on electrically insulating samples. Most electrically insulating samples are coated with a thin layer of conducting material, commonly carbon, gold, or some other metal or alloy. The choice of material for conductive coatings depends on the data to be acquired: carbon is most desirable if elemental analysis is a priority, while metal coatings are most effective for high resolution electron imaging applications. Alternatively, an electrically insulating sample can be examined without a conductive coating in an instrument capable of "low vacuum" operation.

The SEM is carried out by using FEI-Quanta FEG 200-High Resolution Instrument.

Resolution : 1.2 nm gold particle separation on a carbon substrate

Magnification: From a min of 12x to greater than 1, 00,000 X

Application : To evaluate grain size, particle size distributions, material homogeneity and inter metallic distributions.

Sample preparation:

Sample preparation can be minimal or elaborate for SEM analysis, depending on the nature of the samples and the data required. Minimal preparation includes acquisition of a sample that will fit into the SEM chamber and some accommodation to prevent charge build-up on electrically insulating samples. Most electrically insulating samples are coated with a thin layer of conducting material, commonly carbon, gold, or some other metal or alloy. The choice of material for conductive coatings depends on the data to be acquired: carbon is most desirable if elemental analysis is a priority, while metal coatings are most effective for high resolution electron imaging applications. Alternatively, an electrically insulating sample can be examined without a conductive coating in an instrument capable of "low vacuum" operation.

Drug.	**Extract Solvents**	**Colour**	**Nature**	**SEM Particle size in micron**
Rajarajeswaram	Water	Black	Solid	10-15
Madhanabiravam	Water	Pale brown	Solid	1-5

TOXICOLOGICAL EVALUVATION OF RAJARAJESWARAM AND MADHANA BIRAVAM

Introduction

Paracelsus (1493-1541) stated that “All substances are poisons; The right dose differentiates a poison and a remedy” This concept is the fundamental principle of toxicology and hazard assessment.

Medicinal plants play a key role in the human health care because of their efficacy,safety and lesser adverse effects. When herbal drugs are used as a therapeutic substance for treating various ailments, it becomes an essential requirement to fulfill the guidelines formulated by world health organization (WHO). WHO guidelines have given one of the important criteria to establish the safety profile of the herbal preparations.

Hence in the present study the *Rajarajeswaram a*nd *Madhana biravam* tablets were subjected to acute and repeated dose oral toxicity evaluation in order to assess, whether the extracts have any adverse affects or toxic manifestations for long term use. Toxicological study results play the important safety assessment of pharmaceuticals, food additives, pesticides and other chemicals.

In the present toxicological evaluation, the *Rajarajeswaram a*nd *Madhana biravam* were studied in (1)acute oral toxicity study as per the OECD guidelines-423 and (2) 28 days repeated oral dose toxicity study as per OECD Test guidelines 408 .

Materials and Methods

Animals

Wistar albino rats of either sex (140 – 200 gm) were obtained from The King Institute of Preventive Medicine, Guindy, Chennai-600 032. The animals were kept in Animal House, National Institute of Siddha, Chennai-47 and kept in polypropylene cages at 22±2^{o}C with relative humidity 30-70% under 12 hr light and 12 hr dark cycles. They were fed with standard laboratory animal feed (Rodent pelleted feed, Nutrilab rodent, India) and tap water *ad libitum.*

The toxicological protocols were approved by the

IAEC of CPCSEA. (1248/ac/09/CPCSEA/4-10A/2011), (1248/ac/09/CPCSEA/4-10B/2011)

Preparation of the drug for the experimental study

The *Rajarajeswaram a*nd *Madhana biravam* were administered in the form of suspension in water with 30% Twin 80 as suspending agent.

Acute toxicity

Acute oral toxicity study was performed as per OECD-423 guidelines(acute toxic method). Wistar albino rats (n = 3) of female sex selected by random sampling technique was used for the study. The animals were kept fasting for overnight providing only water, after which the *Rajarajeswaram a*nd *Madhana biravam* was administered orally at the dose level of 5 mg / kg body weight by intragastric tube and observed for 14 days. If mortality was observed in 2-3 animals, then the dose administered was assigned as toxic dose. If mortality was observed in 1 animal, then the same dose was repeated again to confirm the toxic dose. If mortality was not observed, the procedure was repeated for further higher doses such as 50, 300 and 2000 mg / kg body weight.

The animals were observed continuously for the first 4 h and then each hour for the next 24 h and at 6 hourly intervals for the following 48 h after administering of the test drug, to observe any death or changes in general behaviour and other physiological activities. Single animals are dosed in sequence usually at 48 h intervals. However, the time interval between dosing is determined by the onset, duration, and severity of toxic signs. Treatment of an animal at the next dose was delayed until one is confident of survival of the previously dosed animal.

Observation of toxicity signs:

General behavior, respiratory pattern, cardiovascular signs, motor activities, reflexes, change in skin and fur, mortality and the body weight changes were monitored daily. The time of onset, intensity, and duration of these signs, if any, was recorded.

28 days repeated oral dose toxicity study

Experimental protocol for 28 days repeated dose study

The following experimental protocol was used to assess the repeated dose oral toxicity study (28 days) of *Rajarajeswaram a*nd *Madhana biravam* in wistar albino rats of either sex .The animals were divided into four groups of six animals each, 3 males and 3 females. 3.96mg,19.8mg and 39.6

Group I - Animals received *Rajarajeswaram* Therapeutic Dose (TD) (3.96mg) daily for 28 days

Group II - Animals received *Rajarajeswaram* 5 X Therapeutic Dose (TD) (19.8mg)daily for 28 days.

Group III - Animals received *Rajarajeswaram* 10 X Therapeutic Dose (TD) (39.6 mg) daily for 28 days**.**

Group IV- Control animals received Tirikaduku kudineer (1ml /kg/po) daily for 28 days.

Body weight, food and water intake were recorded at weekly intervals with simultaneous observation for toxic manifestation and mortality, if any. At the end of 28 days treatment, all animals were sacrificed by cervical decapitation. Blood was collected through retro-orbital puncture and was used for biochemical estimation and hematological studies. Sections of liver, kidney, lungs, heart, stomach and spleen were dissected out and kept in 10 % formalin for histopathological studies.

Group I - Animals received *Madhana biravam* Therapeutic Dose (TD) (1.98mg) daily for 28 days

Group II - Animals received *Madhana biravam* 5 X Therapeutic Dose (TD) (9.9mg) daily for 28 days.

Group III - Animals received *Madhana biravam* 10 X Therapeutic Dose (TD) (19.8 mg) daily for 28 days**.**

Group IV- Control animals received Tirikaduku kudineer 1ml daily for 28 days.

Body weight, food and water intake were recorded at weekly intervals with simultaneous observation for toxic manifestation and mortality, if any. At the end of 28 days treatment, all animals were sacrificed by cervical decapitation. Blood was collected through retro-orbital puncture and was used for biochemical estimation and hematological studies. Sections of liver, kidney, lungs, heart, stomach and spleen were dissected out and kept in 10 % formalin for histopathological studies.

Statistical analysis

The data were expressed as mean ± SEM. Results were analysed statistically by One-Way ANOVA followed by Tukey's multiple comparison using SPSS software student's version. The difference was considered significant if $p<0.05$.

RESULTS AND DISCUSSION

Toxicological evaluvation of *Madhana biravam*

Results and Discussion

Acute toxicity study *Madhana biravam* tablet did not produce any toxic symptoms or mortality at the dose level of 2000 mg/kg/po in rats and hence the drugs were considered to be safe for pharmacological study. According to acute toxic class method (OECD – 423 guidelines) the LD 50 dose of 2000 mg/kg and above is categorized as (X 'unclassified).

28 days repeated oral dose toxicity study

From the observation of the 28 days repeated oral dose study of *Madhana biravam* at the dose of 1.98mg,9.9mg and 19.8 mg did not produce any significant changes in the body weight, food and water intake, No mortality was observed on 1st, 2nd, 3rd and 4th week in both male and female animals of Group I, Group II and Group III and IV. Generally changes in body weight have been used to access the course of the disease and the response to the therapy of drugs and also they indicate the adverse effects of drugs **.** No significant changes were observed in the haematological parameters like Hb, RBC, WBC, clotting time and differential leucocyte counts for *Madhana biravam* treated groups shows the levels of blood glucose, cholesterol, BUN, creatinine respectively. There were no significant changes in any of the hematological parameters in *Madhana biravam* treated group compared with the control groups. The blood glucose level, which remained constant in all the groups of animals, shows the normoglycemic activity of the *Madhana biravam* **.** Determination of BUN and serum creatinine shows that the *Madhana biravam* did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure .

AST, ALT, ALP and total bilirubin are good indices of liver function indicate that there were no significant changes in the enzyme levels, when compared with the control animals. Hence the *Madhana biravam* did not induce any toxicity to the liver and kidney. Determination of kidney function tests shows that the did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure. Hence the *Madhana biravam* did not induce any toxicity to the liver and kidney. This was further confirmed by the histopathological assessment of these organs.

Toxicological evaluvation of *Rajarajeswaram*

Results and Discussion

Acute toxicity study ***Rajarajeswaram*** tablet did not produce any toxic symptoms or mortality at the dose level of 300 mg/kg/po in rats but it produce toxic symptoms and mortality at the dose level of 2000 mg/kg/po in rats ,all three rats were died in 48 hours and Observed of toxicity signs were lethargy, respiration rate reduced, nasal discharge, mild ataxia, gait abnormal mild catalepsy, scratching, diarrhoea, water intake was more and food intake was less, hair straightening, tremor and in necropsy spleen swelling, kidney swelling ,heart normal, both lung reddish colour ,liver mild discolouration, both lung congested, one lung more stasis seen and trachea normal, According to toxic class method (OECD – 423 guidelines) theLD 50 dose of 500 mg/kg and above is categorized as (X 'unclassified).

28 days repeated oral dose toxicity study

From the observation of the 28 days repeated oral dose study of ***Rajarajeswaram*** at the dose of 3.96mg,19.8mg and 39.6 mg did not produce any significant changes in the body weight, food and water intake, No mortality was observed on 1st, 2nd, 3rd and 4th week in both male and female animals of Group I, Group II and Group III and IV. Generally changes in body weight have been used to access the course of the disease and the response to the therapy of drugs and also they indicate the adverse effects of drugs**.** No significant changes were observed in the haematological parameters like Hb, RBC, WBC, clotting time and differential leucocyte counts for ***Rajarajeswaram*** treated groups shows the levels of blood glucose, cholesterol, BUN, creatinine respectively. There were no significant changes in any of the hematological parameters in ***Rajarajeswaram*** treated group compared with the control groups. The blood glucose level, which remained constant in all the groups of animals, shows the normoglycemic activity of the ***Rajarajeswaram.*** Determination of BUN and serum creatinine shows that the ***Rajarajeswaram*** did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure. AST, ALT, ALP and total bilirubin are good indices of liver function indicate that there were no significant changes in the enzyme levels, when compared with the control animals. Hence the ***Rajarajeswaram*** did not induce any toxicity to the liver and kidney. Determination of kidney function tests shows that the did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure. Hence the ***Rajarajeswaram*** did not induce any toxicity to the liver and kidney. This was further confirmed by the histopathological assessment of these organs.

1.Mortality

Observation of 28days sub acute toxicity study of *Madhana biravam* and ***Rajarajeswaram***

Treatment Male /Female	**1st week**	**2nd week**	**3rd week**	**4th week**
Group I	nil	nil	nil	nil
Group I	nil	nil	nil	nil
Group III	nil	nil	nil	nil
Group IV	nil	nil	nil	nil

2.Body weight (gram) observation of 28days sub acute toxicity study of *Madhana biravam* and ***Rajarajeswaram***

Treatment	**1st week**	**2nd week**	**3rd week**	**4th week**
Group I	160.66±6.91	150±9.65	161.33±8.73	168.8±5.40
Group I	165.25 ±10.82	169.33±12.51	174.5±10.80	172.33±7.31
Group III	169.16±9.19	169.66±9.87	173±9.31	169±8.46
Group IV	168.83±6.79	174±5.93	174.66±8.75	172.83±6.11

Values are mean ±SD of respective group of animals.

3. Hematological parameters of 28 days sub-acute toxicity study treatment of *Madhana biravam*

S.No	Parameters	Units	Group I	Group II	Group III	Group III
1	WBC	10^3/mm3	27.56±4.11	24.33 4.77	24.76±5.34	33.18±9.60
2	Lymphocytes%	%	64.78±5.90	60.97±10.34	65.39±2.85	67.58±3.33
3	Monocytes	%	6.74± 0.90	6.80± 1.55	6.34±1.64	4.70± 1.09
4	N/Gr	%	25.36±3.07	26.03± 6.44	24.51±4.59	26.16±4.87
5	RBC	10^6/mm3	7.06± 0.65	7.37 ±0.59	7.01±0.52	7.40± 0.62
6	Hgb	g/dl	15.33±1.06	14.95± 1.15	14.55±1.20	15.41±0.80

Values are mean ±SD of respective group of animals.

4. Biochemical parameters of plasma on 28 days sub-acute toxicity study treatment of *Madhana biravam*

S.no	Parameters	Units	GroupI	GroupII	GroupIII	GroupIV
1.	Albumin	g/ml	4.76 ±0.24	4.58 ±0.37	4.63 ±0.44	5.44±1.2
2.	Bilirubin	mg/ml	0.32 ±0.06	0.32 ±0.08	0.29 ±0.19	0.26 ±0.15
3.	Cholesterol	mg/ml	42.17±5.41	41.55±6.77	44.42±5.62	42.80±6.41
4.	Creatinine	mg/ml	0.65 ±0.03	0.67 ±0.04	0.65 ±0.04	0.65 ±0.03
5.	Glucose	mg/ml	79.71±13.88	87.45±12.17	87.40±8.21	90.79±11.37
6.	Protein	g/ml	6.32 ±0.29	6.25 ±0.41	6.47 ±0.25	6.23 ±0.28
7.	Triglycerides	mg/ml	96.46±21.24	99.10±31.56	73.58±16.12	65.30±22.07
8.	Urea	mg/ml	27.04 ±3.12	26.53 ±2.74	34.83 ±3.17	29.38 ±3.79
9.	AST	U/L	96.80±13.64	106.81±17.08	107.40±17.74	109.19±16.42
10.	ALT	U/L	39.06 ±9.60	41.65 ±8.79	43.04 ±5.64	39. 17±7.82
11.	ALP	U/L	337.50±102.81	408.02±118.38	369.91±75.68	325.6±101.09

Values are mean ±SD of respective group of animals.

5. Hematological parameters of 28 days sub-acute toxicity study treatment of *Rajarajeswaram*

S.No	Parameters	Units	Group I	Group II	Group III	Group IV
1	WBC	10^3/mm 3	8324±312.4	8417±368.1	8542±225.2	7882±361.4
2	Lymphocytes %	%	43.26±2.44	43.28±2.56	44.34±2.2	44.25±2.45
3	Monocytes	%	4.1±0.31	4.2±0.4	4.1±0.4	4.2±0.30
4	N/Gr	%	42.36 ±2.78	43.00±3.1	42.45±3.0	45.10±2.18
5	RBC	10^6/mm 3	5.12±0.35	5.15±0.52	5.44±0.36	5.01±0.32
6	Hgb	g/dl	13.99±0.86	14.2±1.4	14.00±1.2	13.47±0.78

Values are mean ±SD of respective group of animals.

6.Biochemical parameters of plasma on 28 days sub-acute toxicity study treatment of *Rajarajeswaram*

S.no	Parameters	Units	GroupI	GroupII	GroupIII	GroupIV
1.	Albumin	g/ml	2.72±0.05	2.70±0.05	2.75±0.05	2.81±0.07
2.	Bilirubin	mg/ml	0.1±0.02	0.1±0.03	0.1±0.04	0.1±0.03
3.	Cholesterol	mg/ml	57.24±5.52	56.42±5.44	56.19±4.92	56.10±5.10
4.	Creatinine	mg/ml	0.93±0.04	0.92±0.04	0.90±0.04	0.91±0.05
5.	Glucose	mg/ml	80.02±4.48	79.75±3.88	78.62±4.64	82.22±4.10
6.	Protein	g/ml	7.48±0.54	7.42±0.70	7.50±0.72	7.20±0.48
7.	Triglycerides	mg/ml	86.38±2.45	87.42±2.21	88.30±2.58	86.38±3.44
8.	Urea	mg/ml	54.78±3.36	55.42±2.48	54.44±2.12	55.00±2.48
9.	AST	U/L	126.4±5.10	125.4±5.22	127.4±5.72	128.1±5.28
10.	ALT	U/L	34.48±2.99	35.00±2.46	34.92±2.75	35.14±3.15
11.	ALP	U/L	67.10±3.82	66.12±4.30	65.41±4.44	66.11±4.41

Values are mean ±SD of respective group of animals.

Histopathological Evaluation of Madhana biravam

The histopathological studies of the major vital organs like liver, kidney, heart,spleen, lungs, ovary, testis and brain were recovered from both control and *Madhana biravam* treated animals. The histopathological study showed normal architecture suggesting no detrimental changes and morphological disturbances were caused by the daily oral administration of the *Madhana biravam* at the dose level of 1.98mg,9.9mg and 19.8mg for 28 days.

Histopathological studies of the *Madhana biravam* and vehicle treated animals observed mild degenerative changes in liver, lung and kidney. The histopathology results of other organs observed no abnormality detected. Histopathological study showed normal architecture suggesting no detrimental changes and morphological disturbances were caused by the daily oral administration of the *Madhana biravam* at the dose level of 1.98mg,9.9mg and 19.8mg for 28 days.

Histopathological Evaluation of Rajarajeswaram

The histopathological studies of the major vital organs like liver, kidney, heart,spleen, lungs, ovary, testis and brain were recovered from both control and *Rajarajeswaram* treated animals. The histopathological study showed normal architecture suggesting no detrimental changes and morphological disturbances were caused by the daily oral administration of the *Rajarajeswaram* at the dose level of 3.96mg,19.8mg and 39.6mg for 28 days.

Histopathological studies of the *Rajarajeswaram* and vehicle treated animals observed mild degenerative changes in liver, lung and kidney. The histopathology results of other organs observed no abnormality detected. Histopathological study showed normal architecture suggesting no detrimental changes and morphological disturbances were caused by the daily oral administration of the *Rajarajeswaram* at the dose level of 3.96mg,19.8mg and 39.6mg for 28 days.

Histopathological observation of 28 days repeated dose study of Madhana biravam

Groups	**Cytological / Histopathological findings (liver)**
Group I	Mild mononuclear cell infiltration
Group I I	Congestion and biliary epithelial cell hyperplasia
Group III	Sinusoidal congestion, biliary epithelial cell hyperplasia and mononuclear cell infiltration
Group IV	Melild congestion, mild kupffer cell hyperplasia

Histopathological observation of 28 days repeated dose study of Rajarajeswaram

Groups	**Cytological / Histopathological findings (liver)**
Group I	Mild mononuclear cell infiltration
Group I I	Congestion and biliary epithelial cell hyperplasia,mild degeneration of hepatocytes and periportal mononuclear cell infiltration
Group III	Congestion , mild degeneration of hepatocytes , very mild mononuclear cell and neutrphilic infiltration
Group IV	Melild congestion, mild kophilicupffer cell hyperplasia

Histopathological observation of 28 days repeated dose study of Madhana biravam

Groups	**Cytological / Histopathological findings (lung)**
Group I	Mild pulmonary congestion, and mild interstitial mononuclear cell infiltration
Group I I	Pulmonary congestion, oedema,peribronchial and perivascular mononuclear cell infiltration
Group III	Pulmonary congestion, oedema, peribronchial neutrophilic and mononuclear cell infiltration and interstitial mononuclear cell infiltration
Group IV	Mild pulmonary congestion, and mild peribronchial mononuclear cell infiltration

Histopathological observation of 28 days repeated dose study of Rajarajeswaram

Groups	**Cytological / Histopathological findings (lung)**
Group I	Mild pulmonary congestion, and mild interstitial mononuclear cell infiltration
Group I I	Pulmonary congestion, peribronchial mononuclear and neutrophilic infiltration
Group III	Pulmonary congestion, peribronchial mononuclear cell infiltration
Group IV	Mild pulmonary congestion, and mild peribronchial mononuclear cell infiltration

Histopathological observation of 28 days repeated dose study of Madhana biravam

Groups	**Cytological / Histopathological findings (spleen)**
Group I	Mild Congestion
Group I I	Congestion and haemosidrosis
Group III	Congestion and haemosidrosis
Group IV	No abnormality detected

Histopathological observation of 28 days repeated dose study of Rajarajeswaram

Groups	**Cytological / Histopathological findings (spleen)**
Group I	Mild Congestion
Group I I	Congestion and haemosidrosis
Group III	Congestion and haemosidrosis
Group IV	No abnormality detected

Histopathological observation of 28 days repeated dose study of Madhana biravam

Groups	**Cytological / Histopathological findings (kidney)**
Group I	Mild tubular epithelial cell degeneration and very mild interstitial mononuclear cell infiltiration
Group I I	No abnormality detected
Group III	Tubular epithelial cell degeneration
Group IV	Mild tubular epithelial cell degeneration and very mild interstitial mononuclear cell infiltiration

Histopathological observation of 28 days repeated dose study of Rajarajeswaram

Groups	**Cytological / Histopathological findings (kidney)**
Group I	Mild tubular epithelial cell degeneration and very mild interstitial mononuclear cell infiltiration
Group I I	Congestion and tubular epithelial cell degeneration
Group III	Mild tubular epithelial cell degeneration and interstitial mononuclear cell infiltration
Group IV	Mild tubular epithelial cell degeneration and very mild interstitial mononuclear cell infiltiration

Histopathological observation of 28 days repeated dose study of Madhana biravam

Groups	**Cytological / Histopathological findings (stomach)**
Group I	No abnormality detected
Group I I	No abnormality detected
Group III	Glandular stomach- mononuclear cell infiltration in the lamina propria . Non glandular stomach-mild neutrophilic and mononuclear cell infiltration in the lamina propria.
Group IV	No abnormality detected

Histopathological observation of 28 days repeated dose study of Rajarajeswaram

Groups	**Cytological / Histopathological findings (stomach)**
Group I	No abnormality detected
Group I I	Glandular stomach- mild neutrophilic and mononuclear cell infiltration in the lamina propria . Non glandular stomach- No abnormality detected
Group III	Glandular stomach and Non glandular – stomach- mild neutrophilic infiltration in the lamina propria
Group IV	No abnormality detected

Histopathological observation of 28 days repeated dose study of Madhana biravam

Groups	**Cytological / Histopathological findings (Heart)**
Group I	No abnormality detected
Group I I	No abnormality detected
Group III	No abnormality detected
Group IV	No abnormality detected

Histopathological observation of 28 days repeated dose study of Rajarajeswaram

Groups	**Cytological / Histopathological findings (Heart)**
Group I	No abnormality detected
Group I I	No abnormality detected
Group III	No abnormality detected
Group IV	No abnormality detected

ANTICONVULSANT ACTIVITY OF MADHANA BIRAVAM AND RAJA RAJESWARAM AGAINST MAXIMUM ELECTROSHOCK INDUCED SEIZURES IN MALE MICE

INTRODUCTION

Epilepsy has now become the most serious brain disorder, which accounts for about 1% of the world's burden diseases. A number of synthetic anti-epileptic drugs are available in practice, however their effectiveness does not hold true with the entire range of population suffering from this disorder. Further, a large number of drug interactions and their side effects seen with almost all current anti-epileptic drugs make it more difficult to attain easy control on seizures. On the other hand, herbal medicines are widely used across the globe due to their wide applicability and therapeutic efficacy coupled with least side effects, which in turn has accelerated the scientific research regarding the anti-epileptic activity. There is still a need for broad spectrum acting anti-convulsant drugs possessing multiple mechanisms of action with decreased adverse effect, preferably originating from natural products, despite of the beneficial effect of currently available drugs.

Recently, there is a global awareness for the study of traditional system of medicine through application of modern scientific methods. In view of the need for safe and effective drug, the present study was undertaken to evaluate the anti-convulsant effect of the Madhana Biravam and Raja Rajeswaram against the seizures induced by MES (Maximum electroshock) in male mice.

MATERIALS AND METHODS

Drugs

Phenytoin sodium 25 mg (Ranbaxy, India) was used as standard drug in this study and was diluted to the required volume with 2% CMC in saline before use. Appropriate vehicle (Tiri kadugu kudineer) controls were employed wherever necessary. The test drugs also were suspended in 2% CMC to achieve stock concentration and used in this study.

Animals

Swiss albino male mice, weighing between 25 to 30g, two months old were obtained from animal house of Pharmacology department, Vels University. Six animals were housed in each cage made up of polypropylene with stainless steel top grill. The

animals were acclimatized for 7days before commencement of the experiment in standard laboratory conditions 12±01 hour day and night rhythm, maintained at 25 ± 3°C and 50%-70% humidity as per Committee for the Purpose of Control and Supervision of Experimental Animals (CPCSEA) guidelines. Animals were provided with balanced food (Sai meera feeds, Bangalore) and water ad libitum. Protocol used in this study for the use of animals was approved by the institutional animal ethics committee (Approval number: XIII/VELS/PCOL/26/2000/CPCSEA/IAEC/08.08.2012).

Acute toxicity

The acute toxicity study of Madhana Biravam and Raja Rajeswaram up and down-procedure at dose level of 1000 mg/kg and 2000 mg/kg body weight orally in mice as per OECD-425 guidelines was carried out to two groups of mice, each containing six animals and observed for mortality after 24 h.

Dose selection and Stock solution

On the basis of the acute-toxicity results the mice the maximum therapeutic dose of Madhana Biravam and Raja Rajeswaram (MB and RR) was fixed as 250 and 500 mg/kg and 100 and 200mg/kg respectively. The test drugs were suspended in 2% CMC in Saline with suitable concentration (200mg/ml) depending on the body weight of animals and administered orally with the help of oral gavage sleeved to syringe. Phenytoin sodium was selected as standard anti-epileptic drug and administered in the dose of 25 mg/kg.

Evaluation of anticonvulsant activity (MES Model)

Maximal electroshock seizure model was used in the present study to evaluate the anti-convulsant activity of the test drugs. MES seizures were induced by an electro-convulsiometer by delivering electroshock of 60mA current trans-auricularly for 0.2 sec in mice using corneal electrodes. The incidence and duration of extensor tonus were noted. In this type of seizure model, the animals were divided into six groups with six animals and the treatment schedule is as follows.

Group I: Control group- vehicle(Tiri kadugu kudineer 1ml) treated.

Group II: Standard (Phenytoin 25mg/kg)

Group III: Madhana biravam (250mg/kg).

Group IV: Madhana biravam (500mg/kg).

Group V: Raja Rajeswaram (100mg/kg).

Group VI: Raja Rajeswaram (200mg/kg).

The test animals (n=6) received Madhana Biravam (250 and 500 mg/kg) and Raja Rajeswaram (100 and 200 mg/kg) orally 30 min before application of electroshock. To evaluate the drug effect on the seizures severity, the duration of tonic hind leg extension and mortality due to convulsions were selected as the parameters. Each animal was individually observed for 2 hr after MES seizures and at 24 hr for mortality. All the experimental groups were compared with the respective controls treated with vehicle orally.

STATISTICAL ANALYSIS

The duration of tonic hind leg extension phase of MES convulsions expressed as the arithmetic mean ± SE and was analyzed by one-way analysis of variance (ANOVA) followed by Dunnet's 't' test. *P* value less than 0.05 ($P<0.05$) was the criterion for statistical significance.

RESULTS AND DISCUSSION

Epilepsy is a neurological disorder that affects a wide range of people throughout the world. It is a disorder of brain characterized by unpredictable and periodic occurrence of a transient alteration of behavior due to the disordered, synchronous and rhythmic firing of populations of brain neurons. Incidence of epilepsy in developed countries is approximately 50 per 100,000 while that of developing countries, it is 100 per 100,000. It has been observed that the presently available antiepileptic drugs are unable to control seizures effectively. The conventional anti-epileptic agents like Phenytoin, Carbamazepine and Sodium valproate carry with them several serious side effects notably neurotoxicity. As majority of anti-epileptic drugs are consumed life long, concomitant administration of other drugs predisposes to the risk of drug interactions.

However, newer anti-epileptics like Gabapentin, Vigabatrin, Lamotrigine, etc are used supplemental to the conventional agents. Thus, it is necessary to investigate for an anti-epileptic agent that is highly efficacious as well as safe in items of drug related toxicity. The aim of treating an epileptic patient is not only to abolish the occurrence of seizures but also to lead a self sustained life. Although new anti-epileptic drugs have been available since late 1980s, refractoriness to treatment is still an important issue in epilepsy care. Current available anti-convulsant drugs are able to control epileptic seizures efficiently in about 50% of the patients and lead to improvement in another 25% whereas the remainder do not benefit significantly.

Furthermore, undesirable side effects of the drugs used clinically often render treatment difficult; so that a demand for new types of anti-convulsants exists. One of the approaches to search for new anti-epileptic drugs is investigation of naturally-occurring compounds, which belong to new structural classes. In spite of all the marvelous advancements in modern medicine, traditional medicines have always been practiced, because of their natural origin, easy availability, cost effectiveness, lesser side effects, better tolerability, etc. But, because of limited documented experimental evidences regarding their pharmacological effects, the use of traditional medicines remains restricted to a locality/region where they are being practiced traditionally, and not accepted globally.

Several animal models are available that could potentially be used to screen for anti-convulsant activity, but in the present study MES induced convulsion model was used, because this test served as "gold standard" in early stages of drug testing. Seizure refers to a transient alteration of behaviour due to disordered, synchronous and rhythmic firing of populations of brain neurons. Epilepsy is a disorder of brain function characterized by periodic and unpredictable occurrence of seizures. Seizures can be “non-epileptic” when evoked in a normal brain by treatment such as electric shock or chemical convulsants or “epileptic” when occurring without evident provocation. Modern drug therapy of epilepsy is complicated by the inability of drugs to control seizure in some patients and side effects that range in severity from minimal impairment of the central nervous system (CNS) to death from aplastic anaemia or hepatic failure. Thus its effective and safe therapy remains a challenge.

The Madhana Biravam was found to be safe in the doses used and no abnormality in the gross behavioral studies also no mortality were noted in the doses upto 5 g/kg orally but and Raja Rajeswaram exhibited some severe toxic symptoms and mortality at the dose level of 2g/kg. Hence, based on the maximum tolerable dose the one tenth and one twentieth of this dose was considered as therapeutic dose for evaluating further pharmacological study (Anti-convulsant activity using MES model). Since the drug is used clinically for grandmal type of epilepsy this model was employed. This test serves to identify the drug potency that prevents seizure spread, corresponding to generalized tonic-clonic seizures in humans. Electroshock causes the inhibition of GABA release and this, in turn, may inhibit GABA synthesis. All animals treated with (Tiri kadugu kudineer)vehicle exhibited tonic hind limb extension with the electroshock of 60 mA for 0.2sec and the duration of hind limb extension was 20.22 ± 0.29 sec. It has often been stated

that anti-epileptic drugs that block MES-induced tonic extension act by blocking seizure spread, moreover MES-induced tonic extension can be prevented either by drugs that inhibit voltage dependent Na^+ channels or by drugs that block glutaminergic excitation mediated by the *N*-methyl-d-aspartate (NMDA) receptor.

Phenytoin is effective in therapy of generalized tonic-clonic and partial seizures have been found to show strong anti-convulsant action by increasing brain content of Gamma-Amino Butyric Acid (GABA) in MES test. The Madhana Biravam (250 and 500 mg/kg, orally) reduced the incidence of convulsion from 100 to 13.20 and 36.30 % and duration of hind limb extension was reduced to 17.55 ± 0.29 sec and 12.88 ± 0.76 sec ($P<0.01$) respectively, whereas phenytoin abolished the duration of hind limb extension to 11.45 ± 0.82 sec ($P<0.01$) But the mice treated with the Raja Rajeswaram 100 and 200 mg/kg exhibited hindleg extension for 20.00 ± 0.38 and 19.17 ± 0.55sec respectively.

Electroshock causes the inhibition of GABA release and this, in turn, may inhibit GABA synthesis. The most popular and widely used animal seizure model is the traditional MES test. The MES test is considered to be a predictor of likely therapeutic efficacy against generalized tonic-clonic seizures. Thus, our results suggest that test drug may be effective against human generalized tonic-clonic seizures. The Raja Rajeswaram in all doses does not protect animals from seizures but duration of hindleg extension was slightly reduced insignificantly $P> 0.05$ even at a dose level of 200 mg/kg. The rate of protection was very significant at the entire Madhana Biravam treated groups when compared to control.

In the present study treatment with MB and RRK significantly inhibited the MES-induced seizures. Because inhibition of the MES test predicts activity against generalized tonic-clonic and cortical focal seizures, activity against MES-induced seizures suggests that both MB and RRK drugs are useful in suppressing generalized tonic-clonic seizures by regulating GABA-mediated synaptic inhibition. The results were presented in Table 1.

Polypharmacy is often advocated to 30% of all epileptic patients for refractory partial or generalized tonic-clonic seizures. However, none of the new drugs fulfills the ultimate goal of drug treatment of epilepsy, namely complete control of seizures. Therefore, despite the beneficial effect of the currently available drugs, there is still a need for broad-spectrum anti-convulsant drugs possessing multiple mechanisms of action with decreased adverse effect, preferably originating from natural products. The observation in the present study indicated that the Madhana Biravam was without any lethal effect in a dose upto 5 g/kg and the present results indicate that the test drugs exhibited a significant dose dependent protection against electrically induced seizure.

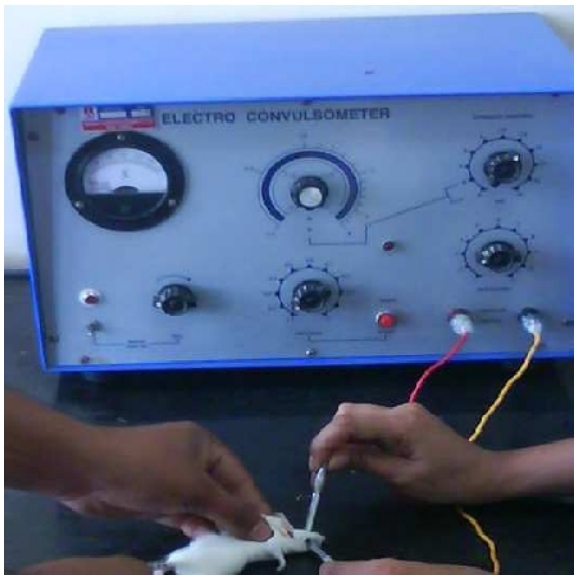


Fig. 2. Effect Of Madhana Biravam And Raja Rajeswaram On Maximal Electroshock (MES)-Induced Seizures In Mice.

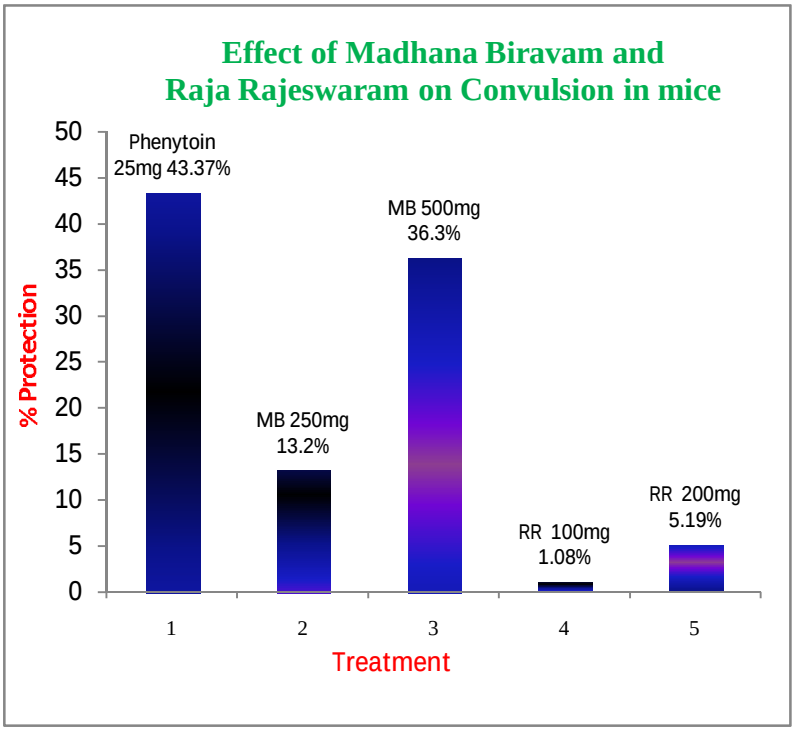


Table: 1. Effect of Madhana Biravam and Raja Rajeswaram on maximal electroshock (MES)-induced seizures in mice

Group and Treatment	Flexor	Extensor	Clonic	Stupor	Death OR Recovery	% Protection
Normal Control (1ml 2% CMC in saline)	1.62 ± 0.11	20.22 ± 0.29	---	---	Death	
Phenytoin (25mg/kg)	1.08 ± 0.61	11.45 ± 0.82**	8.96 ± 0.53	24.29 ± 0.35	Recovery	43.37
Madhana Biravam (250mg/kg)	2.80 ± 0.60[b]	17.55 ± 0.29**[a]	8.17 ± 0.44[ns]	54.21 ± 0.48[a]	Recovery	13.20
Madhana Biravam (500mg/kg)	2.46 ± 0.42[ns]	12.88 ± 0.76**	12.38 ± 0.50[a]	36.51 ± 0.63[a]	Death	36.30
RajaRajeswaram (100mg/kg)	2.87 ± 0.10[b]	20.00 ± 0.38[a]	15.55 ± 0.76[a]	49.49 ± 0.60[a]	Recovery	1.08
Raja Rajeswaram (200mg/kg)	2.99 ± 0.35[b]	19.17 ± 0.55[a]	14.30 ± 0.29[a]	24.25 ± 0.58[ns]	Death	5.19

Values are mean ± SEM. Statistical significant test for comparison was done by ANOVA, followed by Dunnet's 't' test (n=6): The values are *P<0.05, **P<0.01, when compared against control. The values are [a]P < 0.01, [b]P< 0.05, when compared against standard.

CLINICAL STUDY

Aim

To estimate the efficacy of Rajarajeswaram and Madhana biravam in the treatment of valippu(Epilepsy).

Study type: An open clinical trial

Study place: OPD Of Ayothidass Pandithar Hospital, National Institute of siddha, Tambaram sanatorium, Chennai-47.

Population and sample:

20-50 age group fulfilling all the inclusion criteria and passing the exclusion criteria mentioned below.
The sample consists of patients attending the OPD of Ayothidass Pandithar Hospital, National Institute of siddha, Tambaram sanatorium, Chennai-47.

Sample size:

20 patients of both sex

Trial period:

30 days

SUBJECT SELECTION

As and when patients reporting at OPD of Ayothidass Pandithar Hospital with symptoms of inclusion criteria will be subjected to screening test & documented using screening proforma.

INCLUSION CRITERIA

- Agegroup : 20 to 50 Years of both sex
- The symptoms of seizure especially minimum one in 30 days
- Anti –epileptic treatment has to be continued through out the trial period.
- Patient willing to sign the informed consent stating that he/she will conscientiously stick to the treatment during 30days but can opt out of the trial of his/her own conscious discretion.
- Patient willing to attend OPD on every 7th day.
- Patients who are willing to provide blood sample for lab investigation.

EXCLUSION CRITERIA

- Below 20 years, above 50 years.
- Severe uncontrolled epileptic patient.
- The patient history of
    - Pregnancy
    - Lactation
    - Malignancy
    - Cardiac disease
    - Renal failure
    - Liver disease
    - Alcohol intoxication,

WITHDRAWAL CRITERIA

- Intolerance to the drug & development of adverse reactions during drug trial.
- Patient taking medicine irregular & defaulters.
- Patient turned unwilling to continue in the course of clinical trial.
- Increase in severity of symptoms.
- Occurrence of any serious illness.

TEST & ASSESSMENTS

- **CLINICAL ASSESSMENT**
- **SIDDHA ASSESSMENT**
- **ROUTINE INVESTIGATION**
- **SPECIFIC INVESTIGATION**

CLINICAL ASSESSMENT

i. History of epilepsy
ii. Seizure
iii. Body,head and facial spasm.
iv. Bladder incontinence.
v. Bowel incontinence
vi. Tongue bite
vii. Limb jerking and paralysis
viii. Abnormal behavior
ix. Confusion
x. Head ache
xi. Body pain

SIDDHA ASSESSMENT

SIDDHA PARAMETERS

1.Nadi(Pulse perception)

2.Naa(Tongue)

3.Niram(Complexion)

4.Vizhi(Eyes)

5.Mozhi(Voice)

6.Parisam(Palpatory perception)

7.Malam(Bowel habits)

8.Moothiram(Urine){Neerkuri& Neikuri}

ROUTINE INVESTIGATION

- HB (Men-12-15Gms%,Women-11.5-14gms%)
- Total WBC Count(4000-10,000cells/cumm)
- DC- Polymorphs(40-75%)
- Lymphocytes (20-40%)
- Eosinophils (1-6%)
- Monocytes (2-10%)
- Basophils (0-1%)
- Total RBC count(4-6 millions cells/cumm)
- ESR(Men 6-12mm/hr,Women 7-18mm/hr)
- B.glucose (fasting 70-110 mg/dl& post prandial 80-140 mg/dl)
- S. total cholesterol (HDL 30-63mg/dl,LDL 130mg/dl,VLDL 40mg/dl)

RENAL FUNCTION TEST

- B.urea (16-50mg/dl)
- S. total creatinine (0.6-1.2mg/dl)

LIVER FUNCTION TEST

- SGOT(0-40U/dl)
- SGPT (0-35U/dl)
- S.alkaline phosphatase(80-290 U/dl)
- S.uric acid (Men 3-9mg/dl,Women 2.5-7.5mg/dl)

URINE EXAMINATION

- Neerkuri & Neikuri
- Albumin
- Sugar (Fasting & post prandial)
- Deposits

STUDY:

Patients satisfying inclusion and exclusion will be selected for the study. Informed consent will be obtained from the patients before the start of the study. The trail drug will be issued to the patient for 7 days at a time and will be advised to attend OPD after 7 days.

ASSESSMENT FORMS:

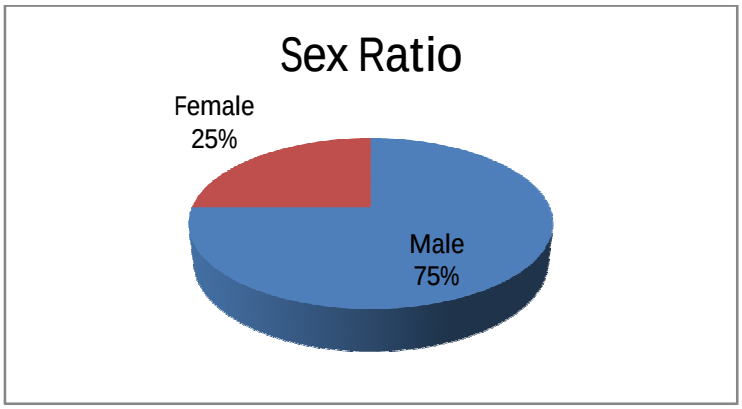
FORM l Screening & Selection Proforma
FORM l A History Proforma On Enrollment
FORM ll Clinical Assessment On Enrollment
FORM ll A Clinical Assessment During & After Trial
FORM lll Laboratory Investigation On Enrollment & Conclusion Of Trial
FORM IV A Consent Form
FORM IV B Withdrawal Form
FORM IV C Patient information sheet
FORM IV D Dietary Advice Form
FORM IV E Adverse Reaction Form

ANALYSIS:

All collected data were entered in the computer and 100% data entry verified through computer system and data analysis carried out by graph pad quick calcs.

RESULTS OF CLINICAL TRIAL

Trial drug:Rajarajeswaram



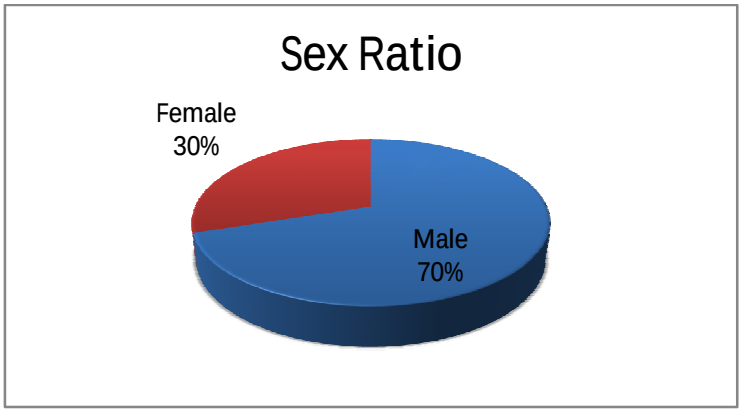
Sex ratio of clinical study

Male patients n = 15(75%)

Female patients n = 05(25%)

Total number of patients = 20

Trial drug:Madhanabiravam



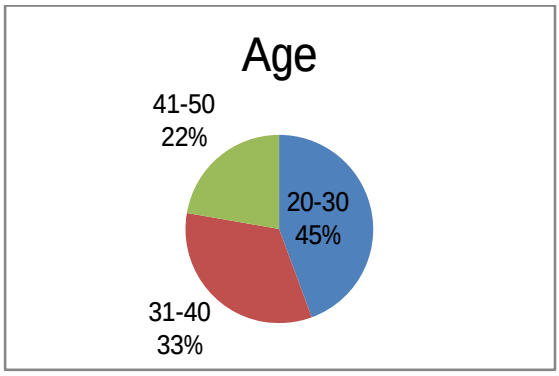
Sex ratio of clinical study

Male patients n = 14(70%)

Female patients n = 06(30%)

Total number of patients = 20

Trial drug:Rajarajeswaram



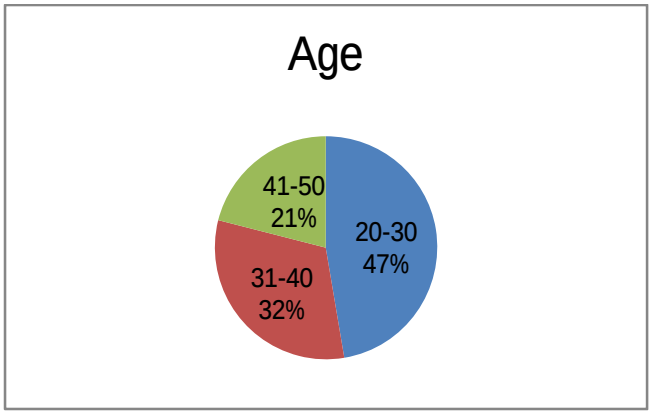
Age wise distribution

20-30 years n =8(45%)

31-40 years n =6(33%)

41-50 years n =4 (22%)

Trial drug:Madhanabiravam



Age wise distribution

20-30 years n =9(47%)

31-40 years n =6(32%)

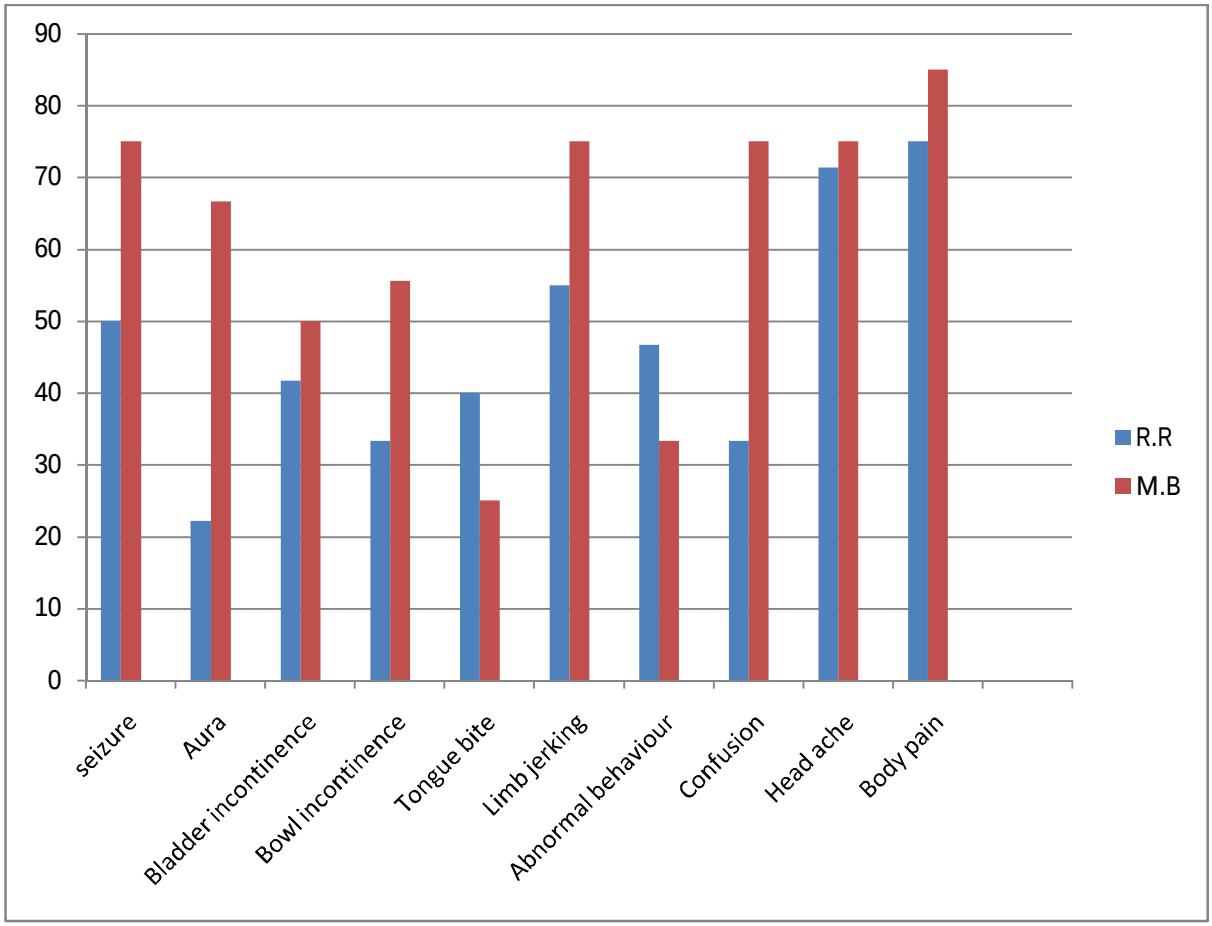
41-50 years n =5 (21%)

Trial drug:Rajarajeswaram

S.No	Symptoms and signs	Before treatment	After treatment trail drug I	Reduction during Treatment	Percentage (%)
1.	Seizure	20	10	10	50%
2.	Aura	09	07	02	22.22%
3.	Bladder incontinence	12	07	05	41.66%
4.	Bowl incontinence	06	04	02	33.33%
5.	Tongue bite	10	06	04	40%
6.	Limb jerking	20	09	11	55%
7.	Abnormal behaviour	15	08	07	46.67%
8.	Confusion	18	12	06	33.33%
9.	Head ache	14	04	10	71.42%
10.	Body pain	20	05	15	75%

Trial drug:Madhanabiravam

S.No	Symptoms and signs	Before treatment	After treatment trail drug II	Reduction during Treatment	Percentage (%)
1.	Seizure	20	05	15	75%
2.	Aura	12	04	08	66.67%
3.	Bladder incontinence	10	05	05	50%
4.	Bowl incontinence	09	04	05	55.56%
5.	Tongue bite	08	06	02	25%
6.	Limb jerking	20	05	15	75%
7.	Abnormal behaviour	12	08	04	33.33%
8.	Confusion	16	04	12	75%
9.	Head ache	16	04	12	75%
10.	Body pain	20	03	17	85%

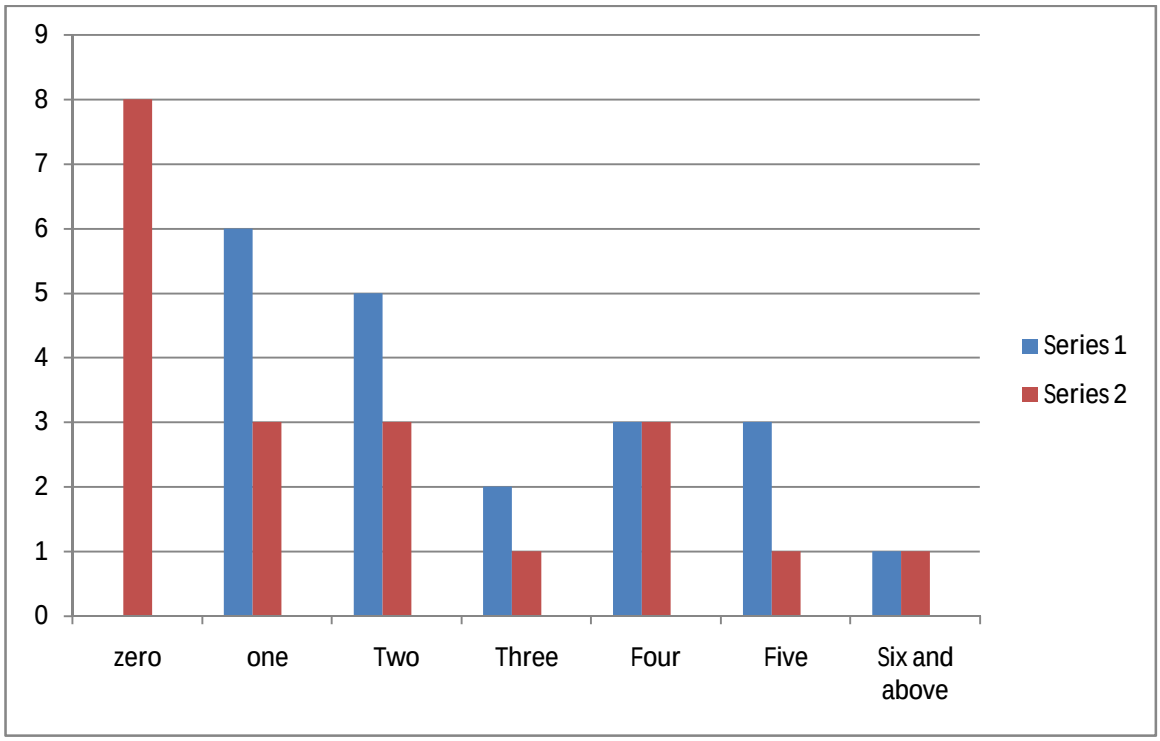


Comparison of signs and symptoms of Rajarajeswaram and Madhana biravam

Trial drug:Rajarajeswaram

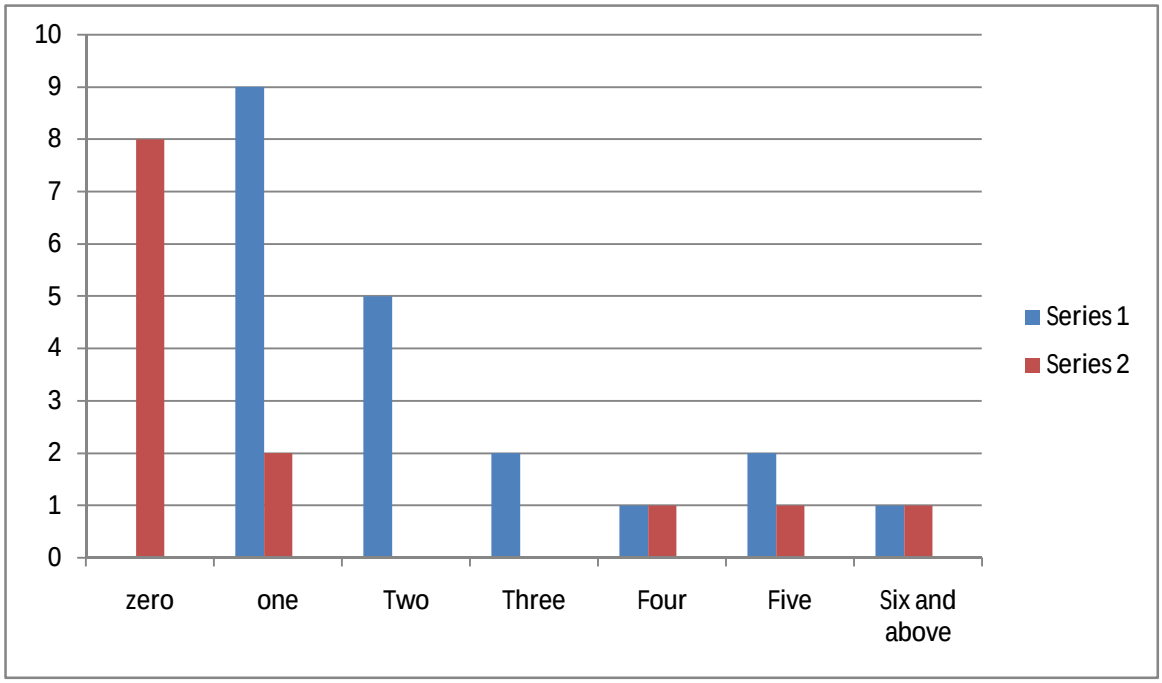
Seizure reduction after treatment

S.NO	Before treatment number of seizure episode in one month	No of patients	After R.R Treatment
	zero	0	08
1	One	6	03
2	Two	5	03
3	Three	02	01
4	Four	03	03
5	Five	03	01
6	Six and above	01	01



Trial drug:Madhanabiravam

S.NO	Before treatment number of seizure episode in one month	No of patients	After M.B Treatment
	zero	0	15
1	One	9	02
2	Two	5	00
3	Three	02	00
4	Four	01	01
5	Five	02	01
6	Six and above	01	01



RajaRajeswaram tablet - Paired *t* test results

P value and statistical significance:
The two-tailed P value is less than 0.0001
By conventional criteria, this difference is considered to be extremely statistically significant.
Confidence interval:
The mean of Group One minus Group Two equals 0.84
95% confidence interval of this difference: From 0.55 to 1.13
Intermediate values used in calculations:
t = 6.0960
df = 18
standard error of difference = 0.138

Review data:

Group	Group One	Group Two
Mean	2.75	1.74
SD	1.65	1.76
SEM	0.37	0.40
N	20	19

Madhana Biravam tablet- Paired *t* test results

P value and statistical significance:
The two-tailed P value is less than 0.0001
By conventional criteria, this difference is considered to be extremely statistically significant.
Confidence interval:
The mean of Group One minus Group Two equals 1.40
95% confidence interval of this difference: From 1.02 to 1.78
Intermediate values used in calculations:
t = 7.6281
df = 19
standard error of difference = 0.184
Review data:

Group	Group One	Group Two
Mean	2.25	0.85
SD	1.59	1.84
SEM	0.35	0.41
N	20	20

OBSERVATIONS AND RESULTS OF CLINICAL STUDY OF RAJARAJESWARAM AND MADHANA BIRAVAM

- Among the 20 cases treated with Rajarajeswaram 75% of patients were male and 25% of patients were female.
- The age distribution of patients treated in this study was as following 45% were in the age group of 20-30 years, 33% were in the age group of 31-40 years,22% were in the age group of 41-50 years.
- Among the 20 cases, 20% of patients taking only Rajarajeswaram tablet and 80% of patients taking Rajarajeswaram tablet along with allopathy medicine.
- From the clinical study 40% patients were reduced from seizure counts.
- 22.22% relived from aura, 40% relived from tongue bite, 55% relived from limb jerking, 46.67% relived from abnormal behavior, 33.33% relived from confusion, 71.42% relived from headache, 75% relived from body pain.
- Some patients had complained drowsiness(40%) and low appetite(35%) and no other adverse effects were observed.
- Among the 20 cases treated with Madhana biravam70% of patients were male and 30% of patients were female.
- The age distribution of patients treated in this study was as following 47% were in the age group of 20-30 years, 32% were in the age group of 31-40 years,21% were in the age group of 41-50 years.
- Among the 20 cases 20% of patients taking only Madhana biravam tablet and 80% of patients taking Madhana biravam tablet along with allopathy medicine.
- From the clinical study 75% patients were reduced from seizure counts. 66.67% relived from aura, 25% relived from tongue bite, 75% relived from limb jerking, 33.33% relived from abnormal behavior, 75% relived from confusion, 75% relived from headache, 85% relived from body pain and no adverse effects were observed.

DISCUSSION

- The trial drugs *Rajarajeswaram* and *Madhana biravam* have been selected for this study to establish its efficacy in the management of valippu(Epilepsy).
- The literature evidence strongly supports the anti- epileptic activity of *Rajarajeswaram* and *Madhana biravam* in the management of valippu(Epilepsy) from the text Siddha vaidiya thirattu, authored by Dr.K.N.Kuppusamy mudaliyar and Dr.K.S.Uhuthamarayan, published by Department of Indian medicine and Homeopathy, Govt of Tamilnadu.
- Chemical analysis of the trial drug ***Rajarajeswaram*** revals the presence of zinc, calcium, magnesium,s ulphate,mercury,arsenic,chloride,oxalate and alkaloids.
- Chemical analysis of the trial drug ***Madhana biravam*** reveals the presence of copper, calcium, magnesium, carbonate,sulphate,mercury,arsenic,chloride,and oxalate.
- The heavy metal analysis of the trial drugs ***Rajarajeswaram*** and ***Madhana biravam*** were permissible limits. Microbial load with in normal limits and aflatoxin not detected.
- The trial drug ***Rajarajeswaram*** IR spectrum showed the presence of hydroxyl group (3404 cm^{-1}), ester carbonyl (2926.5 cm^{-1}), trisubstituted double bond (1626.6 and 830.7 cm^{-1}), aromatic function (1457.6 cm^{-1}) and C-O stretching (1155.5 cm^{-1}).
- The trial drug ***Madhana biravam*** IR spectrum showed the presence of hydroxyl group (3483.7 cm^{-1}), ester carbonyl (2928 cm^{-1}), trisubstituted double bond (1624.4 cm^{-1}) and C-O stretching (1118.1 cm^{-1}).
- Acute toxicity study ***Madhana biravam*** tablet did not produce any toxic symptoms or mortality at the dose level of 2000 mg/kg/po in rats and hence the drugs were considered to be safe for pharmacological study. According to acute toxic class method (OECD – 423 guidelines) the LD 50 dose of 2000 mg/kg and above is categorized as (X 'unclassified).

28 days repeated oral dose toxicity study

- From the observation of the 28 days repeated oral dose study of ***Madhana biravam*** at the dose of 1.98mg,9.9mg and 19.8 mg did not produce any significant changes in the body weight, food and water intake, No mortality was observed on 1st, 2nd, 3rd and 4th week in both male and female animals of Group I, Group II and Group III and IV. Generally changes in body weight have been used to access the course of the disease and the response to the therapy of drugs and also they indicate the adverse effects of drugs. No significant changes were observed in the haematological parameters like Hb, RBC, WBC, clotting time and differential leucocyte counts for ***Madhana biravam*** treated groups

shows the levels of blood glucose, cholesterol, BUN, creatinine respectively. There were no significant changes in any of the hematological parameters in *Madhana biravam* treated group compared with the control groups. The blood glucose level, which remained constant in all the groups of animals, shows the normoglycemic activity of the *Madhana biravam* . Determination of BUN and serum creatinine shows that the *Madhana biravam* did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure .

- AST, ALT, ALP and total bilirubin are good indices of liver function indicate that there were no significant changes in the enzyme levels, when compared with the control animals. Hence the *Madhana biravam* did not induce any toxicity to the liver and kidney. Determination of kidney function tests shows that the did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure. Hence the *Madhana biravam* did not induce any toxicity to the liver and kidney. This was further confirmed by the histopathological assessment of these organs.
- Acute toxicity study *Rajarajeswaram* tablet did not produce any toxic symptoms or mortality at the dose level of 300 mg/kg/po in rats but it produce toxic symptoms and mortality at the dose level of 2000 mg/kg/po in rats ,all three rats were died in 48 hours and Observed of toxicity signs were lethargy, respiration rate reduced, nasal discharge, mild ataxia, gait abnormal mild catalepsy, scratching, diarrhoea, water intake was more and food intake was less, hair straightening, tremor and in necropsy spleen swelling, kidney swelling ,heart normal, both lung reddish colour ,liver mild discolouration, both lung congested, one lung more stasis seen and trachea normal, According to toxic class method (OECD – 423 guidelines) theLD 50 dose of 500 mg/kg and above is categorized as (X ‘unclassified).
- **28 days repeated oral dose toxicity study**
- From the observation of the 28 days repeated oral dose study of *Rajarajeswaram* at the dose of 3.96mg,19.8mg and 39.6 mg did not produce any significant changes in the body weight, food and water intake, No mortality was observed on 1st, 2nd, 3rd and 4th week in both male and female animals of Group I, Group II and Group III and IV. Generally changes in body weight have been used to access the course of the disease and the response to the therapy of drugs and also they indicate the adverse effects of drugs**.** No significant changes were observed in the haematological parameters like Hb, RBC, WBC,

clotting time and differential leucocyte counts for *Rajarajeswaram* treated groups shows the levels of blood glucose, cholesterol, BUN, creatinine respectively. There were no significant changes in any of the hematological parameters in *Rajarajeswaram* treated group compared with the control groups. The blood glucose level, which remained constant in all the groups of animals, shows the normoglycemic activity of the *Rajarajeswaram.* Determination of BUN and serum creatinine shows that the *Rajarajeswaram* did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure. AST, ALT, ALP and total bilirubin are good indices of liver function indicate that there were no significant changes in the enzyme levels, when compared with the control animals. Hence the *Rajarajeswaram* did not induce any toxicity to the liver and kidney. Determination of kidney function tests shows that the did not produce any renal dysfunction, as increase in the above parameters reveals the impaired renal function or acute renal failure. Hence the *Rajarajeswaram* did not induce any toxicity to the liver and kidney. This was further confirmed by the histopathological assessment of these organs.

Pharmacological study

- The pharmacological study suggest that trial drug may be effective against human generalized tonic-clonic seizures. The Raja Rajeswaram in all doses does not protect animals from seizures but duration of hind leg extension was slightly reduced insignificantly P> 0.05 even at a dose level of 200 mg/kg. The rate of protection was very significant at the entire Madhana Biravam treated groups when compared to control.

  The observation in the present study indicated that the Madhana Biravam was without any lethal effect in a dose upto 5 g/kg and the present results indicate that the test drugs exhibited a significant dose dependent protection against electrically induced seizure.
- From the clinical study and statistical analysis proved that the trial drugs *Rajarajeswaram* and *Madhana biravam* is statistically significant response in valippu(Epilepsy).

SUMMARY

- Siddha literatures were revived and collected in support of *Rajarajeswaram* and *Madhanabiravam* for valippu(Epilepsy)and the chosen trial drugs.
- The trial drugs *Rajarajeswaram* and *Madhanabiravam* were prepared as per the standard operative procedures.
- The Physio chemical analysis, FTIR and SEM analysis were carried out and results were obtained.
- *Rajarajeswaram* and *Madhanabiravam* was screened for safety (acute- toxicity, 28 days repeated dose toxicity) and efficacy (Anti -convulsant activity) was carried out as per standard methods. The *Madhanabiravam* was considered to be safe. No mortality, morbidity or adverse changes in the general behaviors in acute toxicity studies. No alterations were observed in haemotological, biochemical parameters and histopathological changes in 28 days repeated oral dose toxicity studies. This shows the drug can be used for long-term administration. But *Rajarajeswaram* produce toxic symptoms and mortality at the dose level of 2000 mg/kg/po in rats ,all three rats were died in 48 hours and Observed of toxicity signs in acute toxicity studies. No alterations were observed in haemotological, biochemical parameters and histopathological changes in 28 days repeated oral dose toxicity studies.
- The anti-convulsant activity of Raja Rajeswaram in all doses does not protect animals from seizures but duration of hindleg extension was slightly reduced insignificantly P> 0.05 even at a dose level of 200 mg/kg. The rate of protection was very significant at the entire Madhana Biravam treated groups when compared to control.
- After obtaining the consent from the patients for the study, the patients were selected from the outpatient department of National Institute of Siddha,Chennai. The trial drug *Rajarajeswaram* and *Madhanabiravam* were administrated to patients those were chosen according to the selection criteria. The patients were carefully observed in regular visit and prognoses were sincerely documented. The trial drug *Madhanabiravam* was able to relive the clinical symptoms of the patients. But compare to *Madhanabiravam* the trial drug *Rajarajeswaram* was less in relive the clinical symptoms and some patients had complained drowsiness and less appetite in trial drug *Rajarajeswaram* and no adverse were observed.

CONCLUSION

The literature evidence, chemical analysis, the toxicological and pharmacological studies and the observation of the clinical studies shows the trial drug Madhana Biravam may be considered as a source in Siddha for therapeutic uses on epilepsy. The Madhana Biravam possess good anti-convulsant activity (500mg)but Raja Rajeswaram have shown moderate activity even at higher dose(200mg) used in this study. Further research is necessary to determine the components involved and their mechanism of action in bringing about the desirable pharmacological effects.

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Lab Parameters Before Treatment- Rajarajeswaram

						D.C %						Blood Sugar (mg/dl)			Serum Cholesterol (mg/dl)				
S.No	OPD/ IPD No	Hb g/dl	T.Rbc Mil/cu	ESR ½ - 1hr	T.Count Cells/cu	P	L	M	E	B	Plt Lak	F	PP	R	Total	HDL	LDL	VLDL	TGL
1.	c-46042	16.2	5.1	2/6	8800	54	45	-	1	-	2.4	-	-	103	199	63	84	52	256
2.	C4335	15.2	5.1	2/6	5100	37	62	-	1	-	1.9	86			220	36	133	51	253
3.	C39362	14.3	4.9	4/8	8900	67	32	-	1	-	3.1	-	-	117	221	38	127	56	279
4.	C39448	14.0	4.9	4/8	11000	60	38	-	2	-	3.2	78	-	-	135	36	78	21	103
5.	C12536	14.1	4.8	2/6	5300	65	28	-	7	-	2.6	80	-	-	203	34	109	36	162
6.	D07874	16.0	5.1	2/6	11000	60	34	-	6	-	2.4	85	-	-	190	54	38	33	120
7.	C83953	14.2	5.0	6/12	7700	60	36	-	4	-	2.9	81	-	-	209	55	42	66	124
8.	C86306	12.4	3.8	8/18	9300	54	40	2	4	-	3.2	99	-	-	178	38	56	48	66
9.	C96356	16.3	5.4	2/4	7400	59	39	-	2	-	2.5	79	-	-	210	42	56	60	875
10.	AK5677	17.1	4.7	2/4	8500	65	29	-	6	-	2.8	96	-	-	247	68	120	66	325
11.	C98318	14.4	4.9	2/10	10600	50	44	2	4	-	1.9	101	-	-	203	46	145	42	263
12.	C88961	13.2	4.7	6/14	6800	65	30	-	5	-	2.6	94	-	-	158	35	106	17	85
13.	C55844	14.4	4.6	4/8	4500	63	32	-	5	-	1.8	76	-	-	165	40	110	15	75
14.	C80893	15.9	4.8	4/8	10500	68	30	-	2	-	2.2	101	-	-	164	30	124	10	50
15.	C78069	14.4	4.6	4/8	6400	58	40	-	2	-	1.8	105	-	-	236	49	174	13	66
16.	C70526	14.8	4.7	4/8	6100	44	52	-	4	-	2.2	94	-	-	179	30	139	10	50
17.	C62597	13.8	5.2	4/8	8200	62	35	-	3	-	3.1	-	-	108	188	35	119	34	170
18.	C72254	15.5	5.4	18/36	5500	44	50	1	5	-	1.4	-	-	103	125	30	87	8	40
19.	C75980	10.9	4.0	6/14	6700	45	49	-	6	-	2.6	82	-	-	182	30	142	10	50
20.	C54605	10.7	3.5	4/10	6800	59	36	-	5	-	2.6	83	-	-	179	30	129	20	100

Lab Parameters Before Treatment-Madhanabiravam

						D.C %						Blood Sugar (mg/dl)			Serum Cholesterol (mg/dl)				
S.No	OPD/ IPD No	Hb g/dl	T.Rbc Mil/cu	ESR ½ - 1hr	T.Count Cells/cu	P	L	M	E	B	Plt Lak	F	PP	R	Total	HDL	LDL	VLDL	TGL
1	c-16024	12.0	3.9	2/6	5600	50	43	2	5	-	3.9	98	-	-	180	31	135	14	72
2	B47751	14.4	4.3	2/3	107000	64	31	-	5	-	2.7	-	-	110	151	30	85	36	183
3	C1512	13.3	4.3	4/8	5500	60	33	1	6	-	1.5	88	-	-	156	37	103	16	81
4	C2007	12.1	3.7	2/4	6500	68	29	-	3	-	2.1	87	-	-	197	30	153	14	74
5	C21510	14.4	4.5	4/8	6600	62	33	-	5	-	2.5	79	-	-	155	24	143	21	105
6	C25212	14.4	4.7	2/4	5800	55	36	1	8	-	2.3	-	-	121	149	30	103	69	345
7	C9709	9.8	3.6	2/16	7500	62	33	-	5	-	2.6	100	-	-	132	24	78	16	81
8	C8992	12.4	4.1	4/8	6000	65	32	-	3	-	2.4	83	-	-	143	26	80	22	114
9	C10744	16.6	3.9	6/17	9500	43	46	1	10	-	3.0	84	-	-	149	30	126	12	63
10	B54563	12	4.5	6/18	5300	50	40	2	8	-	2.1	101	-	-	124	30	42	67	239
11	C5518	12.3	4.0	6/14	9400	65	26	-	9	-		89	-	-	185	38	119	28	138
12	C6961	13.5	4.6	2/8	7500	61	34	-	5	-	3.2	91	-	-	167	39	111	47	185
13	B30157	13.4	4.7	6/12	5800	59	35	1	5	-	2.5	68	-	-	210	45	129	136	182
14	B97750	13.3	4.7	8/18	10300	60	34	-	6	-	2.9	106	-	-	139	32	100	28	141
15	C26409	14.8	5.0	2/8	6400	73	21	-	5	-	2.4	91	104	-	180	41	88	39	197
16	A58602	12.4	4.3	6/20	6800	57	33	1	9	-	2.4	97	-	-	110	27	35	10	50
17	C22973	13.4	4.6	12/24	6700	49	47	-	4	-	2.0	92	-	-	114	27	88	19	97
18	C16024	16.5	5.2	2/10	6700	64	32	-	4	-	2.4	97	131	-	129	30	77	34	170
19	C12536	10	3.4	2/12	7000	55	40	-	5	-	3.6	93	-	-	205	43	97	31	157
20	C22899	15.4	4.7	2/4	8500	54	34	-	2	-	2.9	80	-	-	198	37	87	20	101

Lab Parameters Before Treatment-Rajarajeswaram																
		Blood Group	RFT (mg/dl)			LFT (mg/dl)			Serum (gm/dl)					(IU/L)		
S.NO	OPD/ IPD No	Rh Type	Urea	Creat	U.acid	T.Bil	Dir	Ind	Total	Alb	Glb	Cal	Phos	OT	PT	ALKP
1.	c-46042	O -	21	0.6	6.6	0.6	0.4	0.2	7.6	5.5	2.1	-	-	33	41	155
2.	C4335	O +	15	0.6	5.1	0.8	0.5	0.3	7.3	5.2	2.1	-	-	36	38	180
3.	C39362	O +	29	0.7	9.7	0.6	0.4	0.2	6.9	5.2	1.7	-	-	29	37	144
4.	C39448	O +	17	0.6	3.9	0.5	0.3	0.2	7.9	5.5	2.4	-	-	18	14	159
5.	C12536	O +	23	0.6	-	0.6	0.3	0.3	7.8	5.4	2.4	-	-	23	41	183
6.	D007874	O +	38	0.8	-	0.6	0.3	0.3	8.1	5.8	2.3	-	-	20	17	187
7.	C83953	A +	24	0.7	-	0.5	0.3	0.2	7.7	5.0	2.7	-	-	35	31	116
8.	C86306	B +	16	0.7	-	0.4	0.2	0.2	7.8	4.6	3.2	-	-	20	15	193
9.	C96356	B +	24	0.6	-	0.6	0.3	0.3	7.1	4.0	3.1	-	-	29	30	163
10.	AK5677	A +	28	0.7	-	0.9	0.6	0.3	6.7	3.5	3.2	-	-	34	39	154
11.	C098318	A +	14	0.5	-	0.4	0.2	0.2	7.9	4.9	3.0	-	-	23	25	152
12.	C88961	O +	29	0.8	-	1.0	0.4	0.6	6.3	4.6	1.7	-	-	23	25	164
13.	C55844	B +	16	0.5	-	0.6	0.2	0.4	6.4	4.9	1.5	-	-	24	26	170
14.	C80893	A +	20	0.6	-	0.9	0.4	0.5	6.2	4.9	1.3	-	-	30	28	184
15.	C78069	B +	21	0.7	-	1.4	0.6	0.8	6.9	4.9	2.0	-	-	18	20	185
16.	C70526	B +	24	0.8	-	0.8	0.2	0.6	6.9	4.0	2.9	-	-	13	15	183
17.	C62597	A +	21	0.7	-	0.4	0.2	0.2	7.7	5.1	2.6	9.9	2.8	28	30	204
18.	C72254	A +	16	0.5	-	1.1	0.5	0.6	6.7	4.7	2.0	-	-	19	22	189
19.	C75980	O +	18	0.5	5.5	0.4	0.2	0.2	7.0	5.0	2.0	-	-	32	33	168
20.	C54605	AB +	20	0.6	-	0.4	0.2	0.2	7.1	4.4	2.7	-	-	13	15	170

Lab Parameters Before Treatment-Madhanabiravam																
		Blood Group	RFT (mg/dl)			LFT (mg/dl)			Serum (gm/dl)					(IU/L)		
S.NO	OPD/ IPD No	Rh Type	Urea	Creat	U.acid	T.Bil	Dir	Ind	Total	Alb	Glb	Cal	Phos	OT	PT	ALKP
1.	c-16024	O +	23	0.7	6.0	0.4	0.2	0.2	7.0	5.0	2.0	-	-	27	30	194
2.	B47751	O +	17	0.5	6.0	0.6	0.3	0.3	7.2	4.8	2.4	-	-	25	29	222
3.	C1512	B +	19	0.6	6.7	0.6	0.2	0.4	7.0	4.9	2.1	-	-	18	20	138
4.	C2007	A +	28	0.8	6.0	0.9	0.3	0.6	6.8	4.0	2.8	-	-	34	24	152
5.	C21510	O +	24	0.7	4.2	0.4	0.2	0.2	5.8	3.4	2.4	-	-	22	23	180
6.	C25212	B +	24	0.7	6.2	0.6	0.2	0.4	7.6	5.0	2.6	10.6	2.9	12	14	132
7.	C9709	A +	20	0.6	4.0	0.6	0.2	0.4	7.0	5.0	2.0	11	3.0	19	20	160
8.	C8992	A +	14	0.4	5.9	0.5	0.2	0.3	6.0	4.0	2.0	10.5	3.0	17	18	150
9.	C10744		25	0.8	5	0.5	0.2	0.3	6.9	4.3	2.6	-	-	18	20	135
10.	B54563	B +	19	0.6	5.6	0.4	0.2	0.2	6.2	3.8	2.4	-	-	22	23	160
11.	C5518		20	0.7	2.9	0.6	0.4	0.2	7.1	5.1	2.0	10.7	3.9	27	26	146
12.	C6961		18	0.7	-	0.4	0.2	0.2	6.1	4.6	1.5	-	-	18	20	136
13.	B30157	O +	23	0.7	-	0.6	0.2	0.4	6.9	4.5	2.4	-	-	11	13	156
14.	B97750	O +	16	0.5	3.7	0.5	0.2	0.3	6.5	3.6	2.9	11	3.1	25	26	246
15.	C26409	A1 -	38	1.0	2.9	0.7	0.3	0.4	7.1	4.7	2.4	10.6	2.9	17	19	216
16.	A58602	O +	22	0.6	4.1	0.5	0.2	0.3	5.2	3.2	2.0	-	-	18	19	142
17.	C22973		20	0.6	3.5	0.5	0.2	0.3	7.4	4.0	3.4	10.4	3.0	17	18	184
18.	C16024	A1 +	25	0.6	3.1	0.4	0.2	0.2	6.6	3.7	2.9	11.0	3.1	26	28	195
19.	C12536	O +	19	0.5	3.0	0.4	0.2	0.2	6.6	4.0	2.6	11	3.0	36	27	166
20.	C22899	A +	16	0.5	3.6	0.4	0.2	0.2	7.0	4.0	3.0	10.6	2.8	12	13	160

Lab Parameters Before Treatment- Rajarajeswaram										
S.NO	OPD / IPD No	URINE						Motion		
		AlB	Sug	Pus	Epi	B.S	B.P	Ova	Cyst	Occult Blood
1.	c-46042	NIL	NIL	1 - 2	2 - 3	NIL	NEG	NIL	NIL	NIL
2.	C4335	NIL	NIL	2 – 3	2 - 3	NIL	NEG	NIL	NIL	NIL
3.	C39362	NIL	NIL	3 – 4	3 – 4	NIL	NEG	NIL	NIL	NIL
4.	C39448	NIL	NIL	2 – 3	2 – 3	NIL	NEG	NIL	NIL	NIL
5.	C12536	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
6.	D007874	NIL	NIL	2 – 3	2 – 3	NIL	NEG	NIL	NIL	NIL
7.	C83953	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
8.	C86306	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
9.	C96356	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
10.	AK5677	TRACE	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
11.	C098318	NIL	NIL	1 – 2	2 – 3	NIL	NEG	NIL	NIL	NIL
12.	C88961	NIL	NIL	2 – 3	2 – 3	NIL	NEG	NIL	NIL	NIL
13.	C55844	NIL	NIL	2 – 3	2 - 3	NIL	NEG	NIL	NIL	NIL
14.	C80893	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
15.	C78069	NIL	NIL	0 - 1	1 – 2	NIL	NEG	NIL	NIL	NIL
16.	C70526	NIL	NIL	1 – 2	0 - 1	NIL	NEG	NIL	NIL	NIL
17.	C62597	NIL	NIL	2 – 3	5 - 6	NIL	NEG	NIL	NIL	NIL
18.	C72254	NIL	NIL	2 – 3	2 - 3	NIL	NEG	NIL	NIL	NIL
19.	C75980	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
20.	C54605	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL

Lab Parameters After Treatment -Madhanabiravam

S.NO	OPD / IPD No	URINE						Motion		
		AlB	Sug	Pus	Epi	B.S	B.P	Ova	Cyst	Occult Blood
1.	c-16024	NIL	NIL	1 – 2	2 - 3	NIL	NEG	NIL	NIL	NIL
2.	B47751	NIL	NIL	1 – 2	2 - 3	NIL	NEG	NIL	NIL	NIL
3.	C1512	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
4.	C2007	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
5.	C21510	NIL	NIL	1 – 2	2 - 3	NIL	NEG	NIL	NIL	NIL
6.	C25212	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
7.	C9709	NIL	NIL	3 - 4	3 - 4	NIL	NEG	NIL	NIL	NIL
8.	C8992	NIL	NIL	2 – 3	2 - 3	NIL	NEG	NIL	NIL	NIL
9.	C10744	NIL	NIL	2 - 3	1 – 2	NIL	NEG	NIL	NIL	NIL
10.	B54563	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
11.	C5518	NIL	NIL	4 – 5	5 - 6	NIL	NEG	NIL	NIL	NIL
12.	C6961	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
13.	B30157	NIL	NIL	0 - 1	2 - 4	NIL	NEG	NIL	NIL	NIL
14.	B97750	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
15.	C26409	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
16.	A58602	NIL	NIL	1 – 2	2 - 3	NIL	NEG	NIL	NIL	NIL
17.	C22973	NIL	NIL	4 – 5	4 – 5	NIL	NEG	NIL	NIL	NIL
18.	C16024	NIL	NIL	2 - 3	1 – 2	NIL	NEG	NIL	NIL	NIL
19.	C12536	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
20.	C22899	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL

Lab Parameters After Treatment- Rajarajeswaram

						D.C %						Blood Sugar (mg/dl)			Serum Cholesterol (mg/dl)				
S.No	OPD/ IPD No	Hb g/dl	T.Rbc Mil/cu	ESR ½ - 1hr	T.Count Cells/cu	P	L	M	E	B	Plt Lak	F	PP	R	Total	HDL	LDL	VLDL	TGL
1.	c-46042	16.2	5.1	4/10	9700	52	40	3	5	-	2.0	86	101	-	142	28	71	30	154
2.	C4335	16.4	5.2	2/6	9500	56	38	3	3		2.3	88	106		150	32	70	33	160
3.	C39362	13.3	4.5	2/4	9400	74	20	6	-	-	3.1	-	156	-	208	26	97	68	315
4.	C39448	16.2	5.4	2/4	6100	40	49	2	9	-	2.7	87	-	-	177	30	141	37	174
5.	C12536	13.8	4.8	2/4	5500	60	35	-	5	-	2.7	84	-	-	160	34	101	23	116
6.	D007874	14.3	4.7	20/40	10500	61	31	-	8	-	2.4	77	-	-	131	27	102	31	156
7.	C83953	14.1	5.1	8/16	8100	59	25	1	15	-	3.2	88	-	-	145	30	102	30	164
8.	C86306	17.1	5.2	6/12	4600	65	33	-	2	-	1.5	102	-	-	191	35	82	137	185
9.	C96356	17.4	5.8	2/4	7500	61	36	-	3	-	2.8	74	-	-	193	36	169	55	278
10.	AK5677	16.9	4.8	6/14	7800	58	33	-	9	-	3.0	82	-	-	210	45	128	68	342
11.	C098318	16.2	5.1	8/18	8800	60	32	1	7	-	2.0	82	-	-	132	25	88	52	264
12.	C88961	13.6	4.7	2/12	8100	66	22	2	10	-	2.5	104	-	-	138	24	76	21	108
13.	C55844	14.7	4.4	2/6	6100	58	34	-	3	-	2.6	94	-	-	152	32	96	34	174
14.	C80893	16.9	5.1	2/4	10400	74	23	-	3	-	2.7	-	-	109	140	31	60	25	128
15.	C78069	14.2	4.7	4/10	7300	55	40	-	5	-	2.0	96	163		146	33	68	28	144
16.	C70526	15.1	4.9	2/10	10200	63	33	-	4	-	3.0	-	-	113	200	34	131	26	130
17.	C62597	12.2	4.5	6/18	9300	62	33	-	5	-	3.3	80	-	-	132	26	86	41	208
18.	C72254	16.5	5.6	2/4	4300	49	41	4	9	-	1.5	77	-	-	126	27	50	24	123
19.	C75980	12.9	4.4	10/22	6200	55	42	-	3	-	2.3	98	-	-	152	34	68	54	272
20.	C54605	14.3	3.9	6/12	5500	54	41	-	5	-	2.3	90	-	-	182	36	120	32	112

Lab Parameters After Treatment- Madhanabiravam																			
						D.C %						Blood Sugar (mg/dl)			Serum Cholesterol (mg/dl)				
S.No	OPD/ IPD No	Hb g/dl	T.Rbc Mil/cu	ESR ½ - 1hr	T.Count Cells/cu	P	L	M	E	B	Plt Lak	F	PP	R	Total	HDL	LDL	VLDL	TGL
1.	c-16024	17.6	5.2	2/4	9700	66	22	-	8	4	3.8	101	-	-	168	34	106	36	184
2.	B47751	17.2	5.3	4/8	11100	64	32	-	4	-	3.4	-	-	116	123	28	98	48	244
3.	C1512	16.3	5.2	2/6	6600	63	30	1	6	-	1.3	102	-	-	146	30	102	19	97
4.	C2007	13.1	3.5	2/4	4200	66	30	-	4	-	1.4	81	-	-	200	34	160	30	90
5.	C21510	15.1	4.6	2/4	6300	65	30	-	5	-	2.3	77	-	-	146	38	100	23	115
6.	C25212	14.6	4.7	2/4	5800	55	36	1	8	-	2.3	-	-	121	149	30	103	69	345
7.	C9709	10.6	3.9	4/10	7800	60	35	-	5	-	2.6	92	-	-	108	30	52	16	83
8.	C8992	12.5	4.0	2/10	6600	65	32	-	3	-	2.9	104	-	-	188	42	82	53	266
9.	C10744	17.3	5.5	2/6	5200	52	39	1	8	-	2.1	85	-	-	191	30	102	21	108
10.	B54563	11.5	4.4	2/6	6000	62	33	-	5	-	2.2	106	-	-	231	38	101	22	110
11.	C5518	12.8	3.9	6/12	7600	41	49	1	10	-	-	83	-	-	165	30	70	19	98
12.	C6961	12.9	4.6	2/4	8800	64	30	-	6	-	-	-	-	91	169	27	98	44	220
13.	B30157	13.1	4.5	2/6	5500	50	40	2	8	-	1.8	70	-	-	169	34	80	58	290
14.	B97750	11.5	4.7	2/4	11200	62	33	-	5	-	2.5	-	123	-	138	33	72	37	185
15.	C26409	15.2	5.2	2/4	4800	60	35	-	-	5	1.6	91	-	-	158	34	78	40	485
16.	A58602	11.8	4.6	3/6	9500	50	45	-	5	-	3.0	95	-	-	176	32	102	39	198
17.	C22973	11.9	4.6	6/12	7100	43	45	-	12	-	2.4	104	-	-	177	36	82	34	173
18.	C16024	16.3	5.2	2/4	4900	55	40	-	5	-	2.2	88	-	-	154	32	76	12	63
19.	C12536	12.7	3.3	4/6	7100	55	38	-	7	-	3.2	86	-	-	225	43	112	16	83
20.	C22899	16	4.8	2/4	8400	56	32	-	2	-	3.2	84	-	-	200	36	88	24	90

Lab Parameters After Treatment- Rajarajeswaram															
		RFT (mg/dl)			LFT (mg/dl)			Serum (gm/dl)					(IU/L)		
S.NO	OPD/ IPD No	Urea	Creat	U.acid	T.Bil	Dir	Ind	Total	Alb	Glb	Cal	Phos	OT	PT	ALKP
1.	c-46042	16	0.8	4.7	0.4	0.2	0.2	6.9	4.5	2.4	-	-	20	24	164
2.	C4335	15	0.7	4.5	0.5	0.3	0.2	6.6	4.5	2.1	-	-	20	21	154
3.	C39362	25	0.8	8.6	0.4	0.2	0.2	6.8	3.1	3.6	-	-	50	48	146
4.	C39448	25	0.7	6.7	1.0	0.5	0.5	6.6	4.0	2.6	-	-	15	16	176
5.	C12536	21	0.7	-	0.6	0.2	0.4	6.4	4.2	2.2	-	-	20	25	194
6.	D007874	25	0.8	-	0.6	0.2	0.4	6.9	3.9	3.0	-	-	7	8	243
7.	C83953	17	0.6	-	0.5	0.3	0.2	7.0	5.0	2.0	-	-	22	24	213
8.	C86306	14	0.5	-	0.4	0.2	0.2	6.8	4.8	2.0	-	-	4.-0	26	196
9.	C96356	29	0.8	6.0	0.7	0.3	0.4	6.9	4.0	2.9	-	-	29	30	160
10.	AK5677	21	0.6	5.0	0.4	0.2	0.2	7.6	3.4	4.2	-	-	27	28	180
11.	C098318	21	0.6	5.8	1.3	0.6	0.7	7.2	4.1	3.1	12	3.6	14	15	142
12.	C88961	18	0.5	5.4	0.5	0.2	0.3	5.6	3.6	2.0	11	3.0	11	12	156
13.	C55844	18	0.5	5.7	0.5	0.2	0.3	7.3	5.2	2.1	11.7	3.2	18	19	166
14.	C80893	15	0.5	5.8	1.5	0.6	0.9	6.2	4.2	2.0	10.0	3.1	28	29	170
15.	C78069	23	0.7	8.6	0.5	0.2	0.3	7.7	5.1	2.6	11.4	3.4	22	23	164
16.	C70526	31	0.9	6.1	0.6	0.3	0.3	7.1	5.1	2.0	11.9	3.5	36	28	195
17.	C62597	24	0.7	3.0	0.6	0.2	0.4	7.0	5.0	2.0	11.0	3.2	10	11	145
18.	C72254	14	0.6	4.7	1.4	0.9	0.5	7.4	4.4	3.0	10.0	3.2	25	26	165
19.	C75980	24	0.8	5.9	0.5	0.2	0.3	7.2	5.2	2.0	11.3	3.0	29	30	178
20.	C54605	14	0.4	3.0	0.3	0.1	0.2	6.7	4.7	2.0	10	3	21	31	166

Lab Parameters After Treatment- Madhanabiravam															
		RFT (mg/dl)			LFT (mg/dl)			Serum (gm/dl)					(IU/L)		
S.NO	OPD/ IPD No	Urea	Creat	U.acid	T.Bil	Dir	Ind	Total	Alb	Glb	Cal	Phos	OT	PT	ALKP
1.	c-16024	14	0.4	5.9	0.6	0.2	0.4	7.0	5.0	2.0	11.0	3.0	11	12	150
2.	B47751	14	0.4	5.9	0.5	0.2	0.3	5.5	3.2	2.3	10.2	3.1	15	16	156
3.	C1512	14	0.4	6.5	0.5	0.2	0.3	7.0	5.0	2.0	10.9	3.0	22	19	168
4.	C2007	14	0.4	6.2	0.4	0.2	0.2	6.5	4.5	2.0	12	3.5	19	20	165
5.	C21510	19	0.5	3.2	0.4	0.2	0.2	6.0	3.4	2.6	10.6	3.2	17	19	149
6.	C25212	20	0.6	5.0	0.5	0.2	0.3	5.6	2.8	2.8	10.8	2.9	13	15	146
7.	C9709	14	0.4	3.1	0.4	0.2	0.2	6.1	4.1	2.0	11.5	3.1	12	15	182
8.	C8992	23	0.7	3.4	0.6	0.2	0.4	5.7	3.4	2.4	10.6	3.6	13	15	145
9.	C10744	15	0.6	4.9	0.6	0.2	0.4	7.4	4.0	3.4	10.1	3.9	19	20	168
10.	B54563	14	0.6	4.1	0.6	0.2	0.4	6.7	4.3	2.4	10.8	2.9	16	18	170
11.	C5518	22	0.7	2.3	0.4	0.2	0.2	6.8	4.2	2.6	-	-	29	30	196
12.	C6961	21	0.7	6.0	0.6	0.2	0.4	5.6	3.1	2.5	-	-	15	16	150
13.	B30157	14	0.4	2.6	0.7	0.3	0.4	7.4	4.8	2.6	10.4	3.0	13	14	149
14.	B97750	14	0.5	3.2	0.8	0.3	0.5	6.0	3.9	2.1	10.7	3.0	12	14	152
15.	C26409	15	0.5	4.2	0.4	0.2	0.2	6.3	4.1	2.2	10.7	2.7	49	42	215
16.	A58602	15	0.4	4.1	0.5	0.2	0.3	5.1	3.0	2.1	10	2.9	28	30	194
17.	C22973	15	0.5	4.3	0.6	0.2	0.4	6.2	4.0	2.2	10.9	3.4	20	22	180
18.	C16024	14	0.5	3.3	0.5	0.2	0.3	6.3	4.2	2.1	10.2	3.3	24	26	185
19.	C12536	16	0.6	3.0	0.5	0.2	0.3	5.9	3.3	2.6	10.0	2.8	26	28	183
20.	C22899	16	0.4	3.8	0.4	0.2	0.2	7.2	4.1	3.1	10	2.6	14	16	170

Lab Parameters After Treatment- Rajarajeswaram										
S.NO	OPD / IPD No	URINE						Motion		
		AlB	Sug	Pus	Epi	B.S	B.P	Ova	Cyst	Occult Blood
1.	c-46042	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
2.	C4335	NIL	NIL	1 - 2	2 - 3	NIL	NEG	NIL	NIL	NIL
3.	C39362	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
4.	C39448	NIL	NIL	1 - 2	2 - 3	NIL	NEG	NIL	NIL	NIL
5.	C12536	NIL	NIL	1 – 3	3 – 4	NIL	NEG	NIL	NIL	NIL
6.	D007874	NIL	NIL	2 – 3	2 - 3	NIL	NEG	NIL	NIL	NIL
7.	C83953	NIL	NIL	1 – 2	1 - 2	NIL	NEG	NIL	NIL	NIL
8.	C86306	NIL	NIL	2 – 3	2 - 3	NIL	NEG	NIL	NIL	NIL
9.	C96356	NIL	NIL	1 – 2	1 - 2	NIL	NEG	NIL	NIL	NIL
10.	AK5677	NIL	NIL	3 – 4	2 - 3	NIL	NEG	NIL	NIL	NIL
11.	C098318	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
12.	C88961	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
13.	C55844	NIL	NIL	1 – 2	1 - 2	NIL	NEG	NIL	NIL	NIL
14.	C80893	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
15.	C78069	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
16.	C70526	NIL	NIL	2 – 3	2 - 3	NIL	NEG	NIL	NIL	NIL
17.	C62597	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL
18.	C72254	NIL	NIL	1 – 2	2 - 3	NIL	NEG	NIL	NIL	NIL
19.	C75980	NIL	NIL	1 - 2	1 - 2	NIL	NEG	NIL	NIL	NIL
20.	C54605	NIL	NIL	2 – 4	2 – 4	NIL	NEG	NIL	NIL	NIL

Lab Parameters After Treatment- Madhanabiravam										
S.NO	OPD / IPD No	URINE						Motion		
		AlB	Sug	Pus	Epi	B.S	B.P	Ova	Cyst	Occult Blood
1.	c-16024	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
2.	B47751	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
3.	C1512	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
4.	C2007	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
5.	C21510	NIL	NIL	2 – 3	2 – 3	NIL	NEG	NIL	NIL	NIL
6.	C25212	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
7.	C9709	NIL	NIL	8 – 10	10 - 12	NIL	NEG	NIL	NIL	NIL
8.	C8992	NIL	NIL	4 – 5	2 – 3	NIL	NEG	NIL	NIL	NIL
9.	C10744	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
10.	B54563	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
11.	C5518	NIL	NIL	1 – 2	2 - 3	NIL	NEG	NIL	NIL	NIL
12.	C6961	NIL	NIL	1 – 2	3 – 4	NIL	NEG	NIL	NIL	NIL
13.	B30157	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL
14.	B97750	NIL	NIL	10 – 15	8 - 10	NIL	NEG	NIL	NIL	NIL
15.	C26409	NIL	NIL	2 – 4	3 – 6	NIL	NEG	NIL	NIL	NIL
16.	A58602	NIL	NIL	2 – 3	2 – 3	NIL	NEG	NIL	NIL	NIL
17.	C22973	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
18.	C16024	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
19.	C12536	NIL	NIL	2 – 4	2 - 4	NIL	NEG	NIL	NIL	NIL
20.	C22899	NIL	NIL	1 – 2	1 – 2	NIL	NEG	NIL	NIL	NIL

Rajarajeswaram Raw Drugs & Process

MANOSILAI

LINGAM

PAAL THUTTAM

NAABI

GANDHAGAM

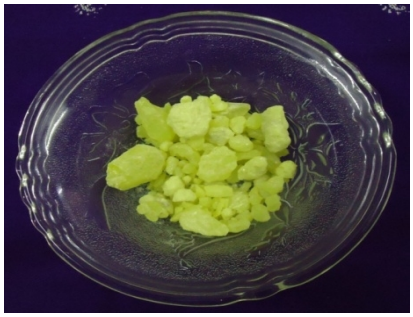
RASAM

PICHU

GRINDING

VILLAI

Madhanabiravram Raw drugs & process

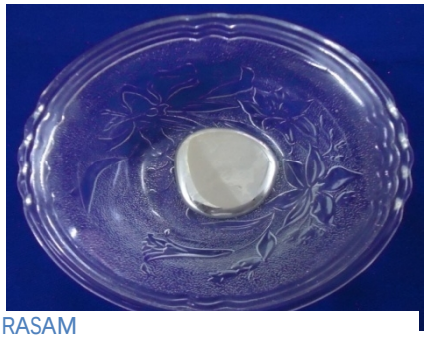


GANDHAGAM

INDHUPPU

TAAMIRA THAGADU

MANOSILAI



RASAM

TAAMIRA PARPAM

PICHU

GRINDING

PUDAM

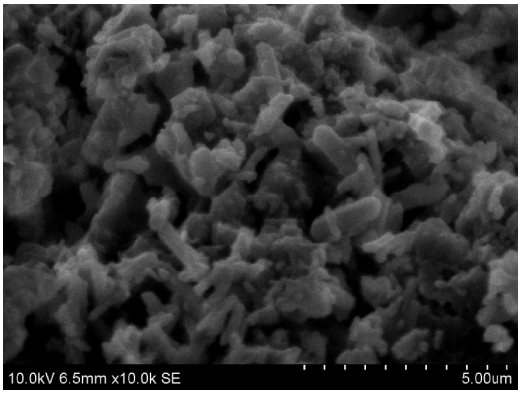
VILLAI

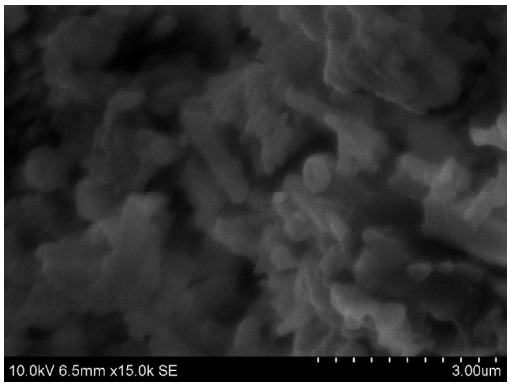
RAJARAJESWARAM

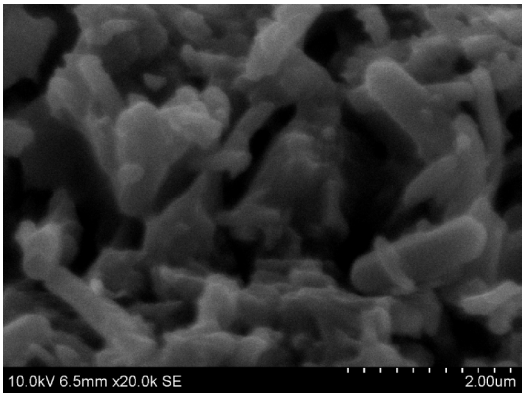
MADHANABIRAVAM

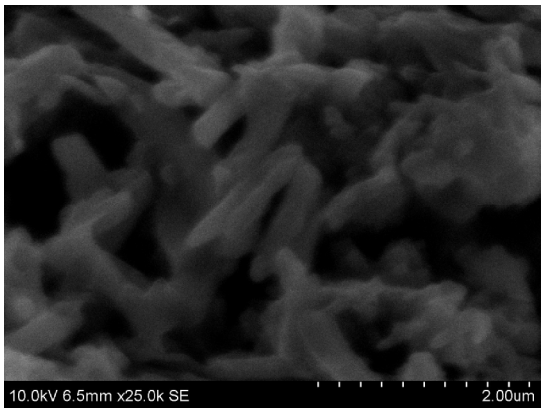
SEM ANALYSIS-

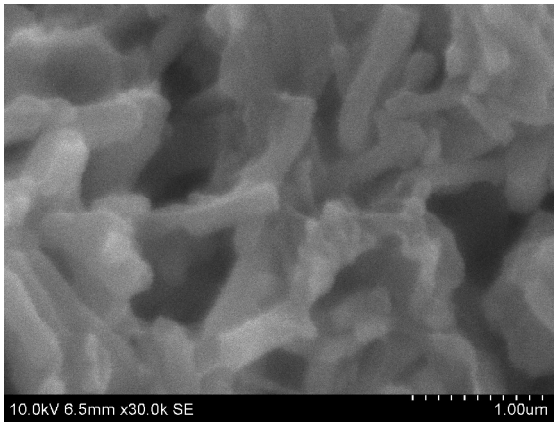
RAJARAJESWARA KULIGAI





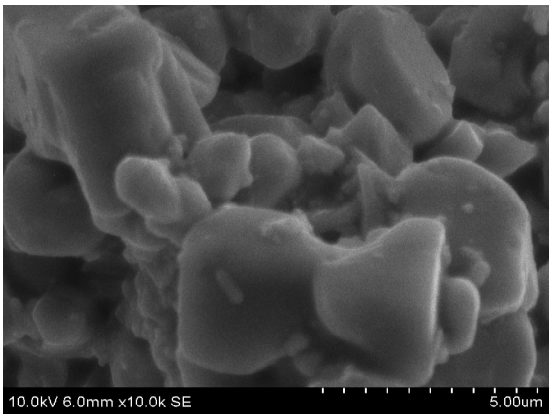


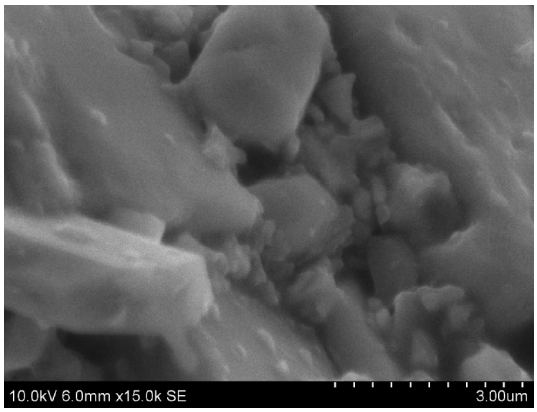


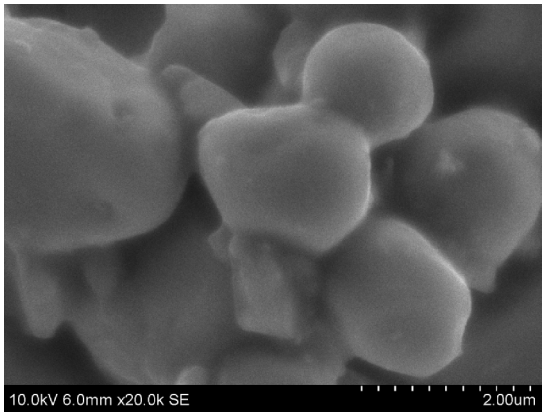


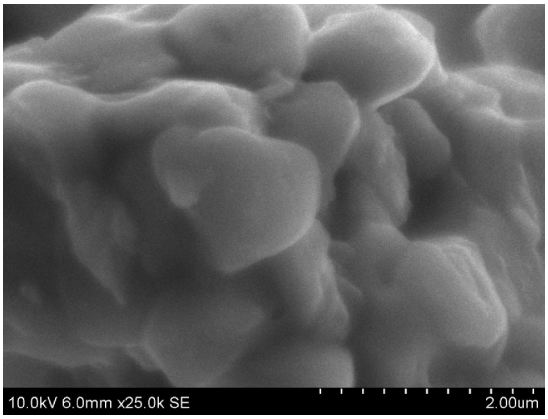
SEM ANALYSIS

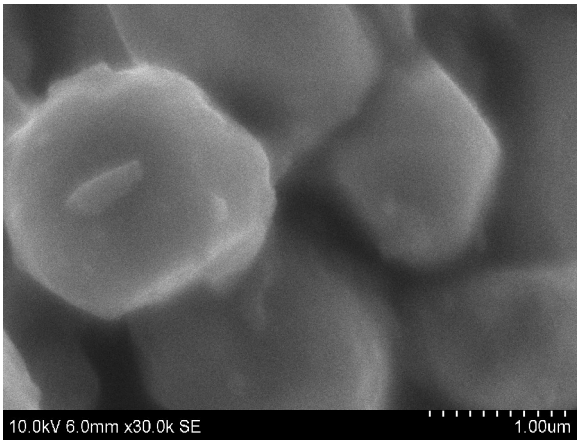
MADANA BIRAVAM





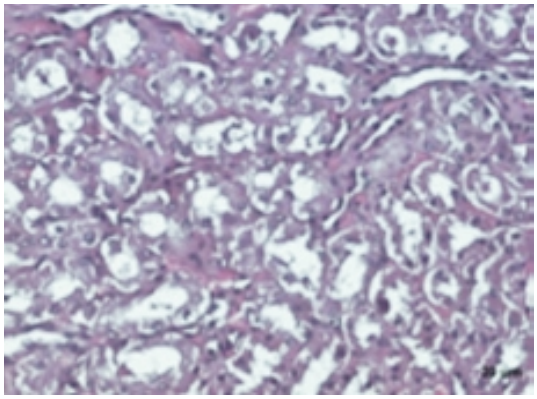




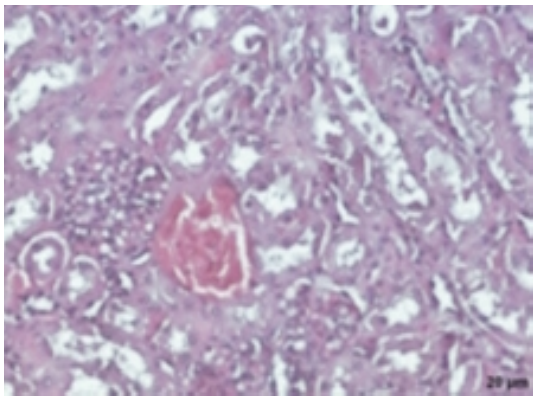


MADHANA BIRAVAM

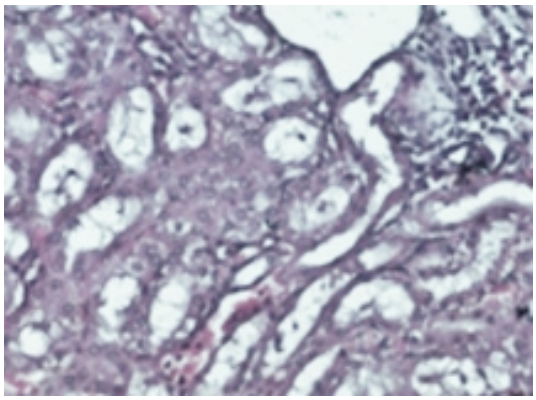
Sub-acute toxicity kidney-I



Kidney-II

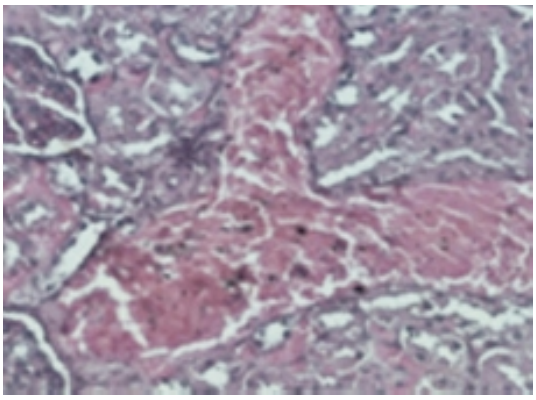


Kidney-III

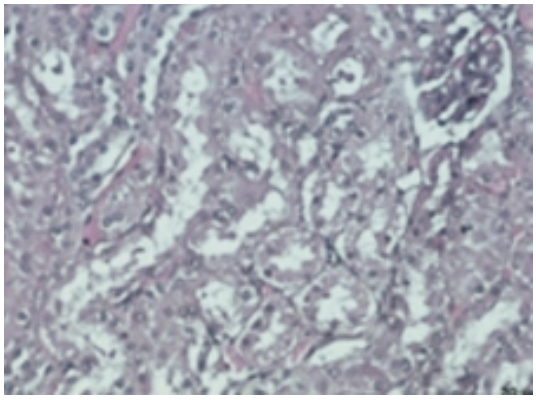


RAJARAJESWARAM

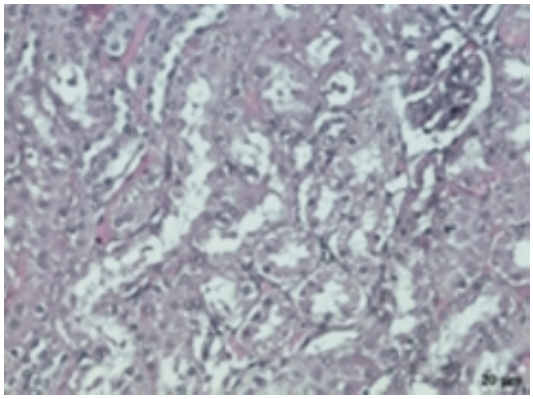
Sub-acute toxicity kidney-I



Kidney-II



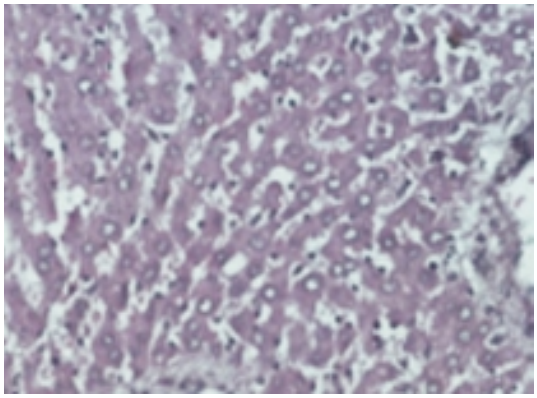
Kidney-III



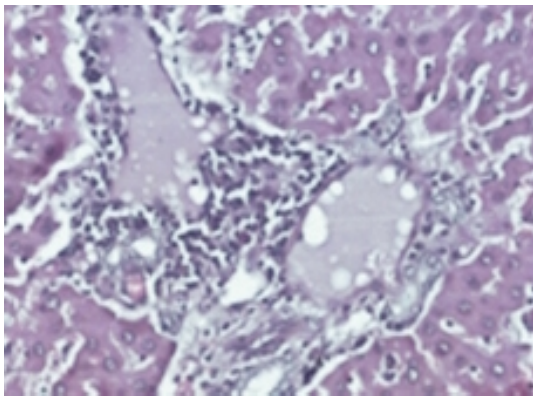
Kidney-IV

MADHANA BIRAVAM

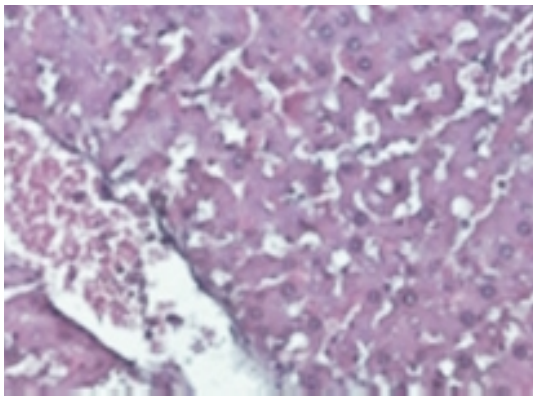
Sub-acute toxicity Liver-I



Liver-II

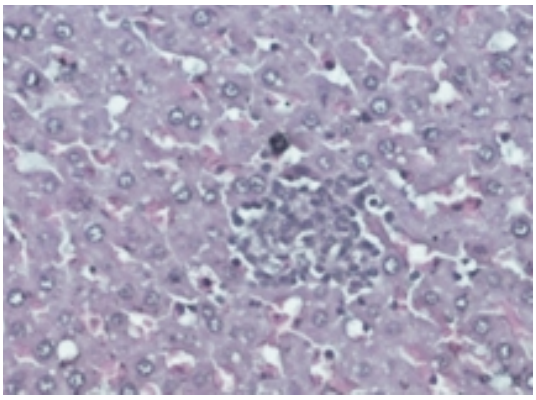


Liver-III

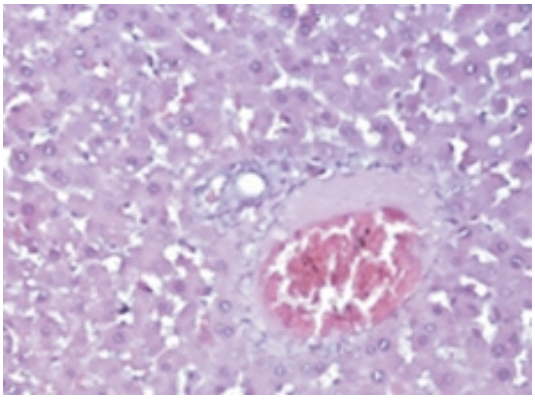


RAJARAJESWARAM

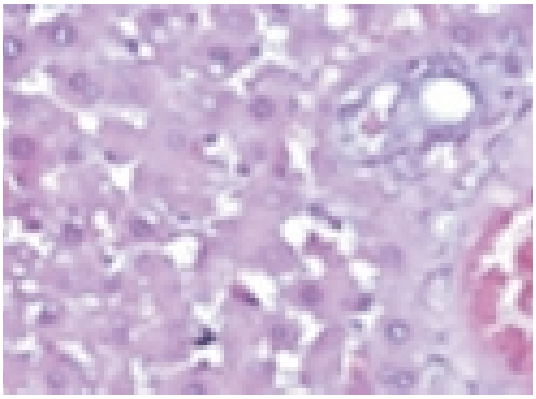
Sub-acute toxicity Liver-I



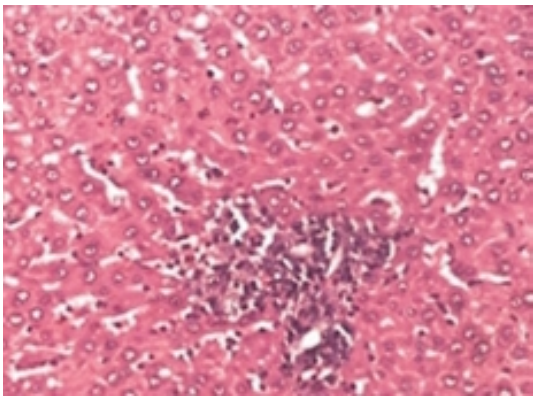
Liver-II



Liver-III

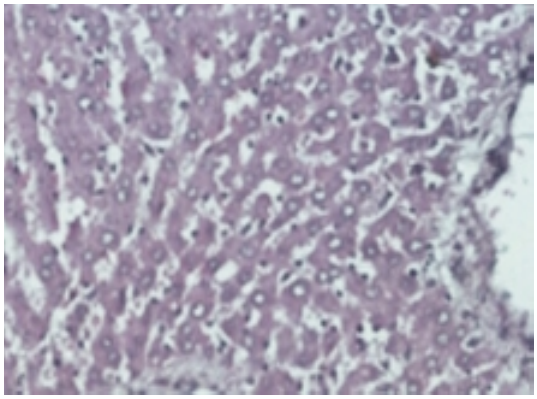


Liver-IV

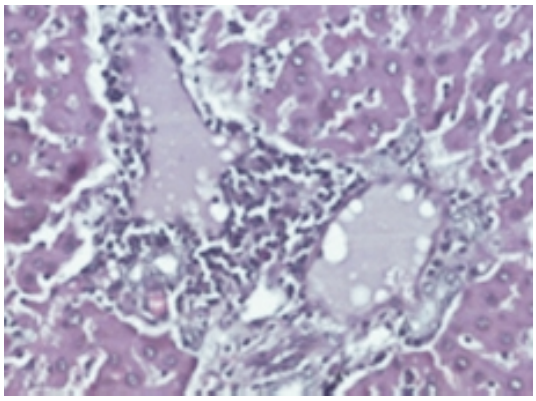


MADHANA BIRAVAM

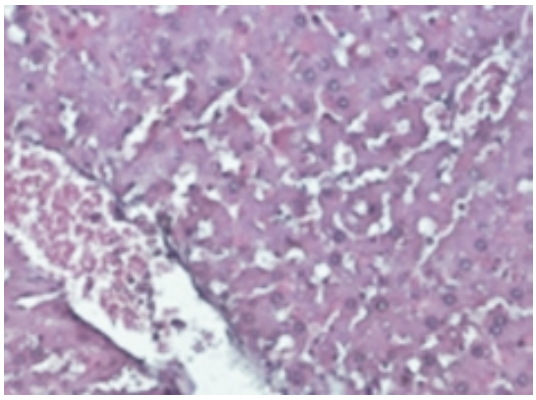
Sub-acute toxicity Lung-I



Lung-II

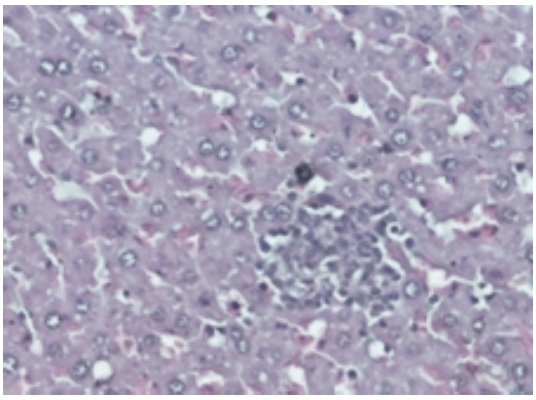


Lung-III

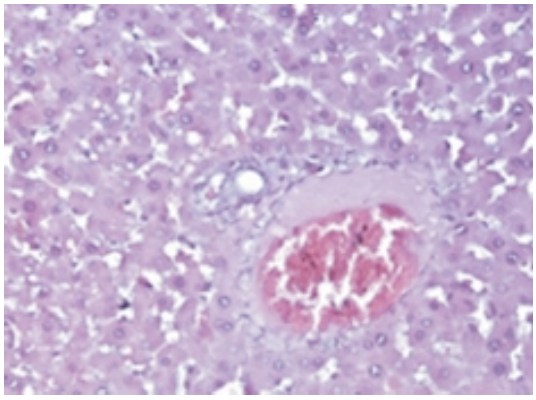


RAJARAJESWARAM

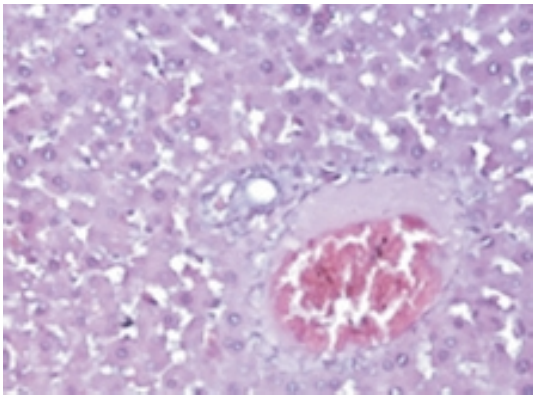
Sub-acute toxicity Lung-I



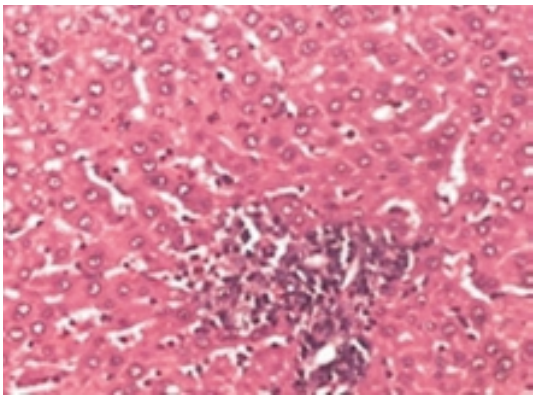
Lung-II



Lung-III

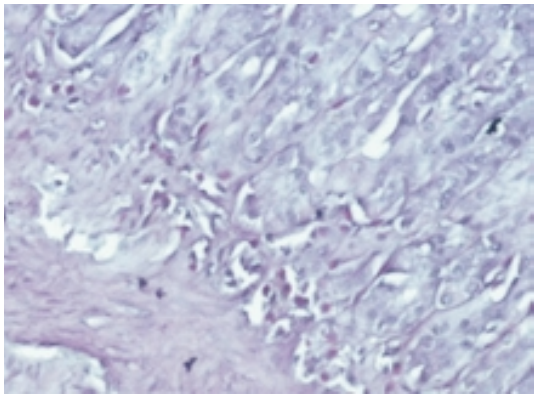


Lung-IV

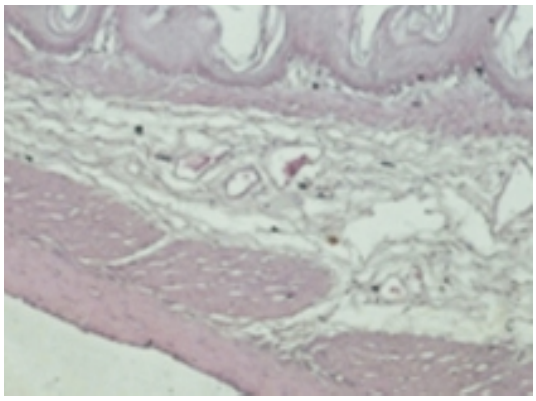


MADHANA BIRAVAM

Sub-acute toxicity Stomach-I



Stomach-II



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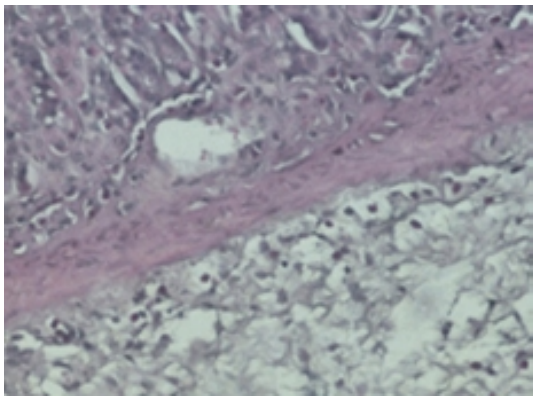
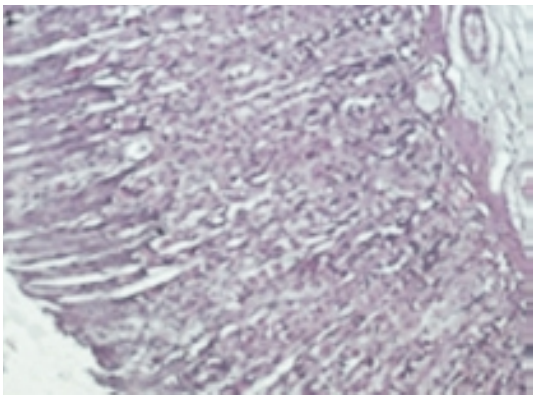
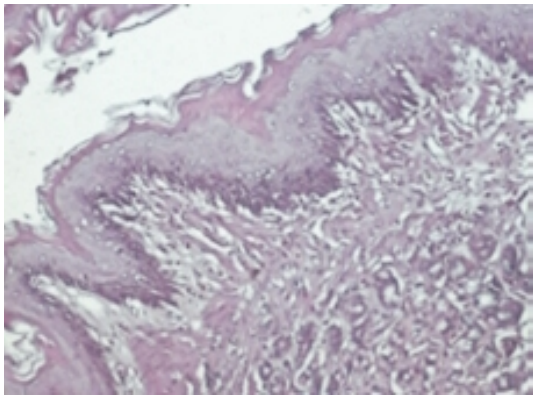


RAJARAJESWARAM

Sub-acute toxicity Stomach-I



Stomach-II



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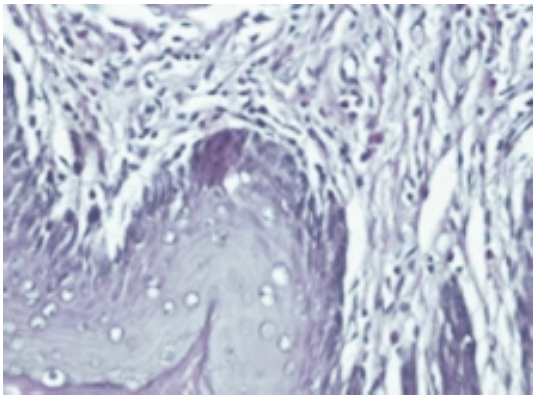
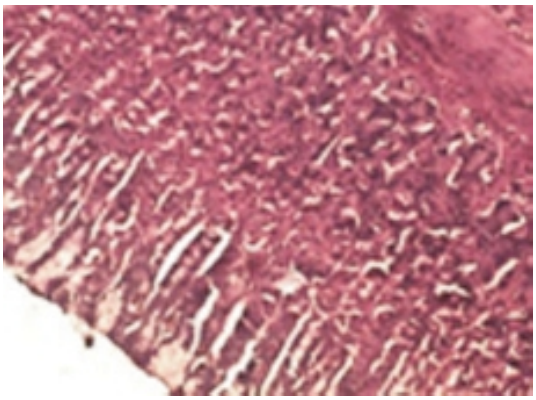
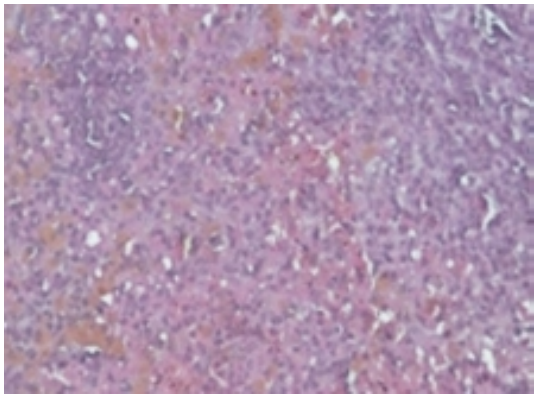


Stomach-IV

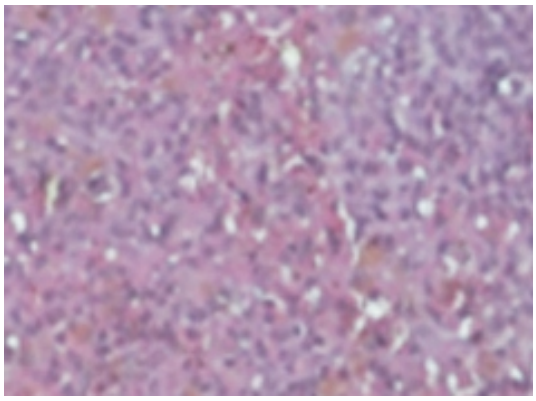


MADHANA BIRAVAM

Sub-acute toxicity Spleen-I



Spleen-II



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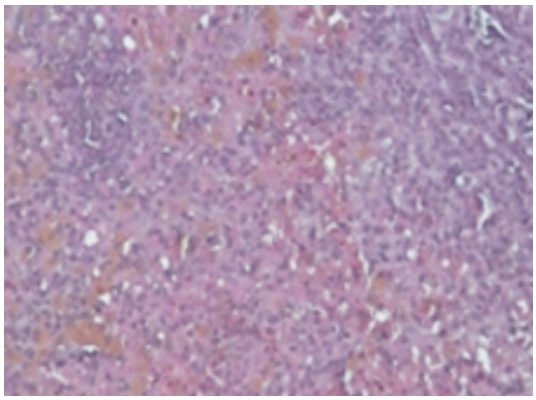
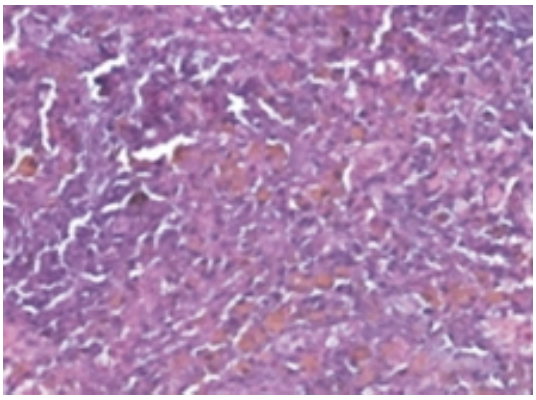
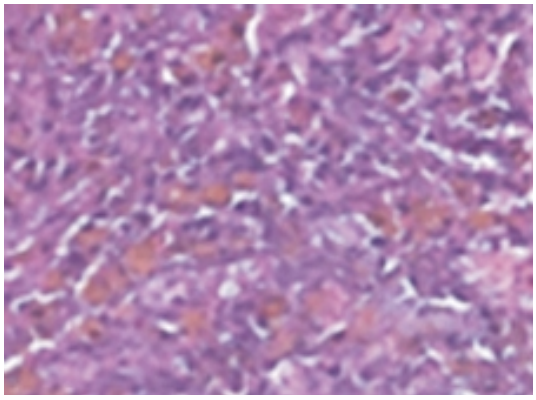


RAJARAJESWARAM

Sub-acute toxicity Spleen-I



Spleen-II



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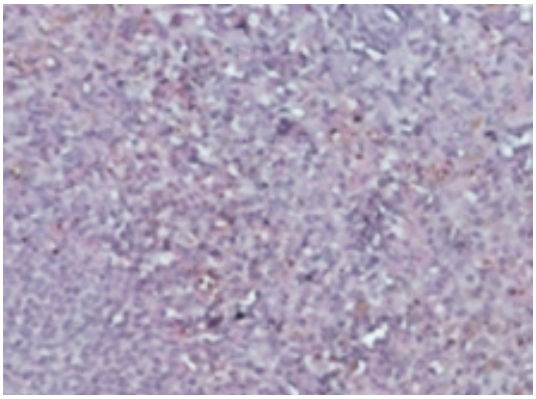
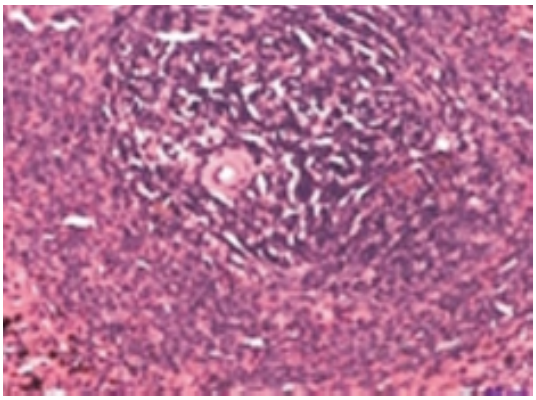
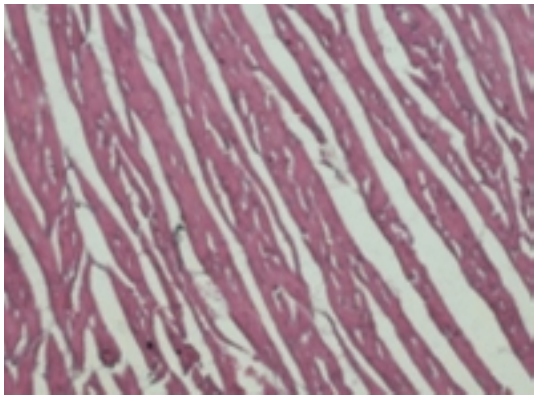


Spleen-IV

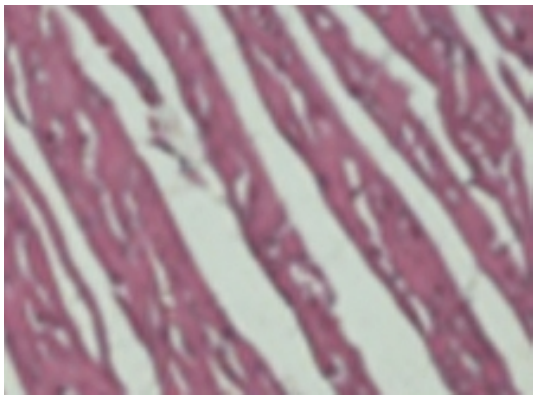


MADHANA BIRAVAM

Sub-acute toxicity Heart-I



Heart-II



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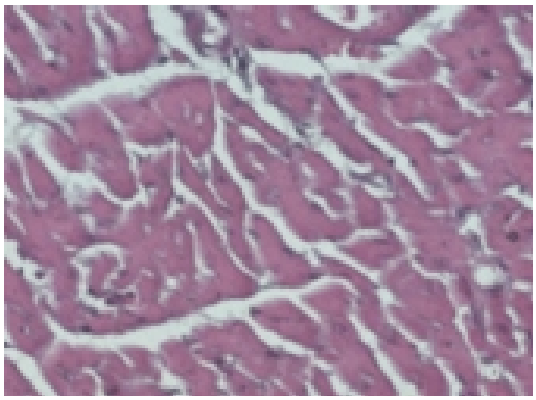
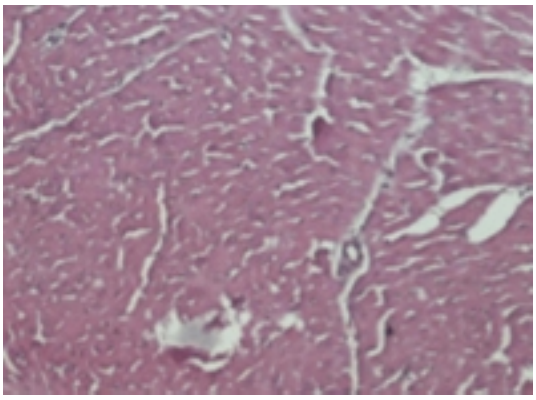


RAJARAJESWARAM

Sub-acute toxicity Heart-I



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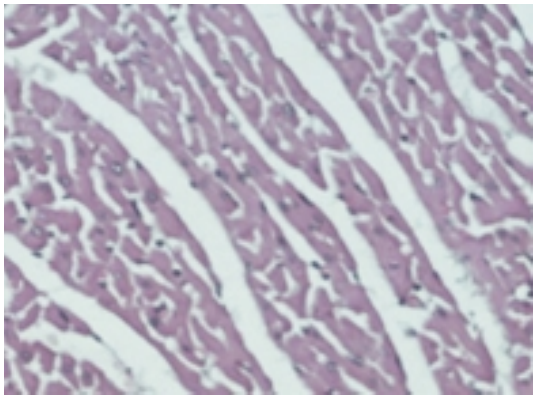
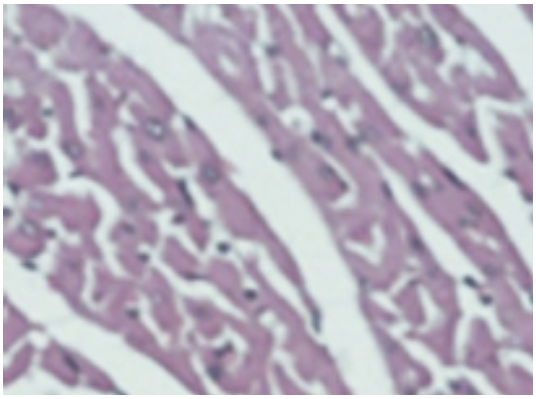
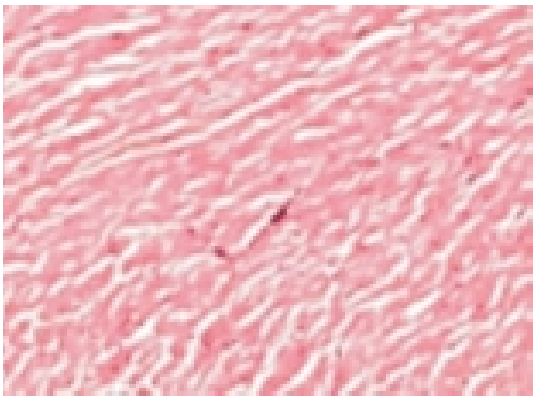


Heart-III



Heart-IV



TAMIL NADU VETERINARY AND ANIMAL SCIENCES UNIVERSITY

Referral Laboratory for Diagnostic Cytology and Histopathology (RLDCH)
Department of Veterinary Pathology
Madras Veterinary College, Chennai - 600 007, India.

Phone : 91-44-2538 1506 Extn.: 288 **Fax : 91-44-2536 2787** **Grams : VETDEAN**

Ref. No. : Nil./Dated.22.10.2012
Received on 22.10.2012

Date: 22.11.2012

RESULTS

S. No.	Lab. No.	Sample No.	Tissues	Cytological / Histopathological Findings
1.	1378-83/12	Rat, Rajarajeswara Kuligar Group II	Liver (1No.)	Congestion and biliary epithelial cell hyperplasia
			Lung (1No.)	Pulmonary congestion, oedema, peribronchial and perivascular mononuclear cell infiltration
			Spleen (1 No.)	Congestion and haemosiderosis
			Kidney and heart, stomach (each 1 Nos.)	No abnormality detected (NAD)
2.	1384-89/12	Rat, Rajarajeswara Kuligar Group III	Liver (1No.)	Sinusoidal congestion, biliary epithelial cell hyperplasia and mononuclear cell infiltration
			Lung (1No.)	Pulmonary congestion, oedema, peribronchial neutrophilic and mononuclear cell infiltration nd interstitial mononuclear cell infiltration
			Spleen (1 No.)	Congestion and haemosiderosis
			Kidney (1 No.)	Tubular epithelial cell degeneration
			Stomach (1 No.)	Glandular stomach-Mononuclear cell infiltration in the lamina propria
				Non glandular stomach-Mild neutrophilic and mononuclear cell infiltration in the lamina propria
			Heart (1 No.)	No abnormality detected (NAD)
3.	1390-95/12	Rat, Madhana Biravam Group II	Liver (1No.)	Congestion and biliary epithelial cell hyperplasia, mild degeneration of hepatocytes and periportal mononuclear cell infiltration
			Lung (1No.)	Pulmonary congestion, peribronchial mononuclear and neutrophilic infiltration
			Spleen (1 No.)	Congestion and haemosidrosis
			Kidney (1 No.)	Congestion and tubular epithelial cell degeneration
			Stomach (1 No.)	Glandular stomach- Mild neutrophilic and mononuclear cell infiltration in the lamina propria
				Non glandular stomach- No abnormality detected (NAD)
			Heart (1 No.)	No abnormality detected (NAD)
4.	1396-401/12	Rat, Madhana Biravam Group III	Liver (1No.)	Congestion, mild degeneration of hepatocytes, very mild mononuclear and neutrophilic infiltration
			Lung (1No.)	Pulmonary congestion and peribronchial mononuclear infiltration
			Spleen (1 No.)	Congestion and haemosidrosis
			Kidney (1 No.)	Mild tubular epithelial cell degeneration and interstitial mononuclear cell infiltration
			Stomach (1 No.)	Glandular stomach and non glandular stomach - Mild neutrophilic infiltration in the lamina propria
			Heart (1 No.)	No abnormality detected (NAD)

To
Dr.A.Kirubakaran,
National Institute of Siddha, Chennai-600 047

for Principal Investigator
Scheme Code No. 18018
and Professor and Head
Department of Veterinary Pathology
Madras Veterinary College,
Chennai-600 007
22/11/12

e-mail : dchl_mvcpat@yahoo.com

Regional Research Institute of Unani Medicine (RRIUM)
(Central Council for Research in Unani Medicine, New Delhi)
No.1, West Madha Church Road, Royapuram, Chennai – 600 013.
☎ Office: 25955519; Fax: 25955532

TEST CERTIFICATE

Issued to	: Dr. A. Kirubagaran, National Institute of Siddha, Department of Gunapadam, National Institute of Siddha, Tambaram, Chennai – 600 047
Ref. No.	: Your Letter No. 3.07.2012
Test report as per	: Customer requistion
Report No.	: 2012-13/dated 29.11.2012

PART - A: PARTICULARS OF SAMPLE RECEIVED

a. Name od the sample	**: Mathana Biravam**
b. Grade/variety/type/size/class etc	: Nil
c. Declared values, if any	: Nil
d. Code No	: Nil
e. Batch No. and Date of manufacture	: Nil
f. Quantity	: 50 g
g. Mode of packing	: Plastic container
h. Seal	: Not intact
i. Sample received on	: 3.07.2012

PART – B: SUPPLEMENTARY INFORMATIONS

a. Reference to sampling procedure	: Drawn and supplied by customer
b. Supporting documents for the measurements taken and results derived	: Nil
c. Deviation from the test methods as prescribed in relevant ISS/Work instructions, if any	: Nil

4. Analysis of Microbial Load

The procedures recommended for analysis of Microbial Load as per WHO, 1998.

S. No.	Parameters	Results	Permissible Limit for Internal use
1	**Total Bacterial Count (TBC)**	**< 10 CFU/g**	**10^5 CFU/g**
2	**Total Fungal Count (TFC)**	**< 10 CFU/g**	**10^3 CFU/g**
3	**Enterobacteriaceae**	**Absent**	**10^3 CFU/g**
4	***Escherichia coli***	**Absent**	**10 CFU/g**
5	**Salmonella Spp**	**Absent**	**Absent**
6	***Staphylococcus aureus***	**Absent**	**Absent**

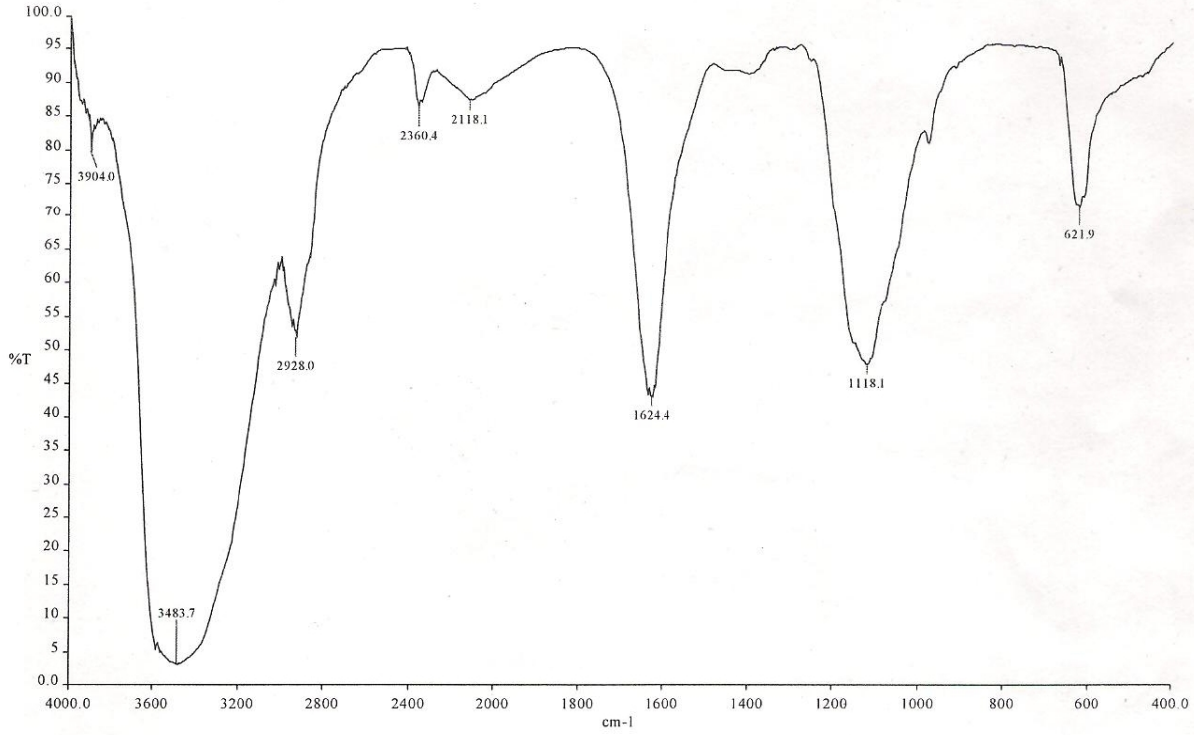
NB:

1. The results stated above relate only to the items tested.
2. This test certificate shall not be reproduced except in full without the written approval of the laboratory.
3. The test report shall not be utilized for any legal purpose without prior intimation to the issuing authority.

P. Meera Devi Sri
Consultant (Microbiology)

Dr. D. Ramasamy
Research Assistant (Chemistry)

Dr. Rampratap Meena
Research Officer (Chemistry) – S2



Kirubhakaran Madhana bairavan 17.10.12.pk

KIRUBH~2.SP 3601 4000.0 400.0 3.1 100.0 4.0 %T 4 2.0

PT

REF 4000 100.0 2000 90.1 600

3904.0 79.8 3483.7 3.1 2928.0 51.9 2360.4 86.3 2118.1 87.4

1624.4 43.1 1118.1 48.0 621.9 71.7

END 8 PEAK(S) FOUND

18/10/12

Professor and Head
Department of Chemistry, CEGC
Anna University, Chennai-600 025.

Issued to :

Dr.A. Kirubagaran M.D (S)
Gunapadam Branch
National Institute of Siddha
Tambaram Sanatorium
Chennai – 47.

SARGAM LABORATORY PVT. LTD.
F2, Thiru-Vi-Ka Industrial Estate,
(Phase-III Ekkattuthangal) Guindy, Chennai - 600 032.
Phone : +91 44 - 4967 4000, 4967 4001
Fax : +91 44 - 4967 4001
Email : enquiry@sargamlabs.com
sr@sargamlabs.com
accounts@sargamlabs.com
Website : www.sargamlabs.com

Recognised by BIS, AYUSH
Approved by Drug Controller of India, EIC, APEDA, AGMARK (Export) and FSSAI

TEST REPORT

SUBMITTED SAMPLE

Report Number : M135946
Lab Code No. PF12-10-184-02

Report Date : 09.10.2012

Page : 1 of 1

Sample Name : Madhana Biravam

Received on : 08.10.2012

Commenced on: 09.10.2012

Customer's Reference : Letter dated 03.10.2012

Completed on : 09.10.2012

TEST	OBSERVED RESULT
Description	Pale Brown colour pellets
Disintegration time	7 minutes 10 seconds

.....End.....

Report prepared by: G. Lakshmi

Verified

Authorized Signatory

P. GOPAL
Technical Manager

Terms and Conditions :

* The test results relate only to the items tested. * The test report shall not be reproduced in full or part without the written approval of SLPL. * The test items will not be retained for more than 15 days from the date of issue of test report in the case of perishable items and 3 months in the case of metal samples unless otherwise agreed with the customer or as required by the applicable regulation. * The Laboratory's responsibility under this report is limited to proven willful negligence and will in no case be more than the invoiced amount.

IAEC PROTOCOL NO: 1248/ac/09/CPCSEA/4-10A/2011

20/12/2011

CERTIFICATE

This is certify that the project title Preclinical and Clinical Study on MADHANABIRAVAM" for Anti-EPILEPTIC activity in the Mangnoot of Valippu [EPILEPSY] **has been approved by the IAEC.**

Prof. Dr. K. Manickavasakam — **Name of Chairman/Member Secretary IAEC:**

Dr. B. Jayachandran Dare — **Name of CPCSEA nominee:**

Signature with date

Chairman/Member Secretary of IAEC:

CPCSEA nominee:

(Kindly make sure that minutes of the meeting duly signed by all the participants are maintained by Office)